HEREDITY IN MAN

BY

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TO

MY WIFE

THIS BOOK IS AFFECTIONATELY DEDICATED

PREFACE

In the last five years there has been an enormous increase in the scientific output on human heredity, and the quality of the medical publications on inherited abnormalities and diseases has greatly improved. The younger generation of medical practitioners have had some acquaintance with the general principles of Mendelian inheritance, with the result that the quality of their writings, from the point of view of the investigator of heredity, is much better. But still the importance of recording accurately all the normal as well as abnormal descendants or ascendants and relatives of an affected individual is not always realised. In the earlier medical literature, pedigrees are put on to paper in every conceivable form, so that the sophisticated reader, instead of being able to see at a glance the method of inheritance, must usually decipher a unique set of symbols and puzzle out the relationships.

It will be a great advantage in the future if something like uniformity of symbols and pedigree construction is adopted more widely than at present, although there has been great improvement in this respect. The method adopted in this book is not necessarily better than any other, but at any rate it is clear, easily understood and widely used—a square representing a male, a circle a female, the square or circle being black when the particular condition is present, and white in its absence. Of course, the publisher of a pedigree often finds it desirable to use additional symbols for various purposes, to indicate individuals personally examined, a condition which may be present only on the right or left side, etc.

The great increase in the scientific literature on human inheritance has necessitated a complete revision of my book, and its title has been altered in accordance with the contents. Several chapters of the previous work are omitted altogether. The remainder, except the Introduction, are fully revised, largely rewritten, and very extensively added to. The chapters on physical and mental inheritance in man have been broken up into several and rearranged owing to the large increase in material; and chapters have been added on the blood

groups, metabolic defects, and racial crossing. It is proposed to include a chapter on twins and the inheritance of twinning in a future edition, but the subject is hardly ripe for treatment at the present moment, although much has been written in the last few years.

Chapters IX. and XVI. in particular have been written from the anthropological point of view and really represent applications of genetics to anthropology. This is another field in which great advances have taken place in the last few years, most of the material in these two chapters being only recently available, and some of the facts not previously published.

It is impossible to cite more than a tithe of the papers bearing on heredity in mankind. Only a selection of the more important or pertinent papers is given. Complete citations are less necessary, as full bibliographies of the current literature are to be found in such publications as the *Zeits. f. ind. Abst.- u. Vererbungslehre*, *Resumptio Genetica*, *Bibliographia Eugenica* (published in the *Eugenical News*), and *Biological Abstracts*.

For notes on the individuals in Fig. 69, as well as the photograph, I am indebted to Dr. E. B. Sherlock.

Regarding illustrations, the number of pedigrees has been largely extended and those illustrating particular points have been chiefly chosen, the more lengthy ones being too bulky for reproduction here. I am indebted to the Royal Anthropological Institute for permission to reproduce Figs. 75-79 from my paper on Amerind Crosses in Canada in *Journ. Roy. Anthrop. Inst.*, vol. lviii., part ii., and Figs. 80-81 from *Man*, vol. xx.; to Dr. J. P. Lotsy for prints of Figs. 83-87; and to Messrs. J. Springer for permission to use Figs. 12-16 from Weidenreich's *Rasse und Körperbau*.

Finally, I am indebted to many correspondents for kindly sending me their papers bearing on human heredity, and to Dr. H. E. Bargmann for abstracting some of the papers.

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33, WOBURN SQUARE, W.C. 1,
April 20, 1929.

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HEREDITY IN MAN

CHAPTER I

INTRODUCTION

The central problem of evolution is still the nature and causes of variation, while the practical problems of Eugenics centre about heredity. Variation in past ages has already endowed the human race with an almost infinite variety of types and characters, many of the latter alternative in their inheritance. We have only to compare those we know best with their relatives and ancestors to realise how minute are the resemblances and differences which may be handed on to descendants and collateral lines. These are, no doubt, chiefly a matter of biological inheritance, though similarity of environment may play a part in certain cases. Probably in no other species of animal or plant does the number of differences between individuals approach the number to be observed in man. This is to be expected, because of the mental and physical complexity of the human organism; but it does not imply greater intrinsic variability than in other animals or plants.

Given this enormous complexity of types in the human species, and the inheritance of the innumerable differences involved, it follows that the matings of the present generation determine the characteristics which will be handed on to future generations. A knowledge of inheritance must, therefore, form the basis of any enlightened attempt to influence the future development of the human race, which Sir Francis Galton originally contemplated in the Eugenic Movement. Popular writers frequently venture to deny the importance of heredity to mankind. They are willing to concede its cogency in animals, and, in fact, practical breeders of horses and dogs and other domestic animals rely upon heredity to perpetuate even slight differences in their strains. But they are often unwilling to accept for mankind the principles of heredity which they themselves have practised or seen in operation in

other animals. Even those who recognise that the principles of heredity must be the same for mankind as regards physical characters, are sometimes inclined to deny that the same laws hold for mental characteristics.

It is therefore hoped that this book may help to bring the reader to a truer perspective regarding the nature and meaning of heredity, and its fundamental bearing on the future of the human race. False conceptions regarding inheritance are widespread, and this is not surprising in view of the complexity of the subject and the general lack of education in the biological sciences. Only in the last two decades, through experimental investigations with plants and animals, has any clear road been found through a mass of complicated data. It may now be claimed, however, that the general mechanism of heredity is well understood in many cases, and although, as in every science, complications continually arise with further knowledge, the principles already understood will form a sound basis for future advance.

It is impossible in this book to consider the whole field of heredity in general terms. For that purpose, reference may be made to various works on the subject which have appeared in recent years, during which the field of genetics has been an extremely active one. In this work an effort will be made to bring together the more important facts on human heredity which have accumulated chiefly in the last twenty years; but the general principles will be briefly discussed, and reference will be made to experiments, particularly with regard to the higher animals, when the results bear directly upon problems of human heredity. It will be seen that a large amount of information has been gained regarding the inheritance of a multitude of traits, both physical and mental, in mankind. And perhaps the most surprising feature of these results is the minuteness and variety of the differences which are now known to follow definite laws of inheritance. But it is not necessary to rely upon recent work to establish the minuteness and peculiarity of some of the differences which are inherited in man. Darwin, who was unsurpassed as an observer, and, what is equally important, a collator of the observations of others, has a chapter on blushing in his book, *The Expression of the Emotions*, in which (p. 312) he cites, not only a number of cases of the inheritance of a tendency to blush, but also one in which mother and daughter blushed in the same peculiar manner. The tendency to blush excessively is due

to a psychological peculiarity, while the distribution of the area over which a blush spreads must have a physical basis. That gait, gestures, voice, and general bearing are inherited, was recognised in the scientific writings of over a century ago, though imitation may also, of course, play a part here, but this is excluded in some cases.

Further random examples of inheritance in man will not be cited here, but the reader is invited to consider the mass of evidence found in the body of this book. It is believed that, in this way, any reader who is inclined to doubt the universality and importance of heredity in mankind will attain a truer perspective regarding the whole matter. But certain misconceptions need to be pointed out first. The question is often asked whether heredity or environment is more important in connection with development. But the question cannot rightly be asked in this way, because any organism is the result of continuous complicated reactions and interactions, not only between the developing germ and its environment, but also between the different parts of the organism itself. Moreover, it is quite incorrect to assume that the organic germ and the environment mutually react with each other in any simple way. A particular change in the environment may conspicuously affect one part of the developing organism without visibly affecting other parts. Thus Stockard (1909) showed that when magnesium chloride is added to the sea water in which certain fish embryos are developing, cyclopean fishes are produced, with one median eye instead of two lateral ones. This is a surprising reaction of the organism, and more particularly of the nervous system, to a definite environmental stimulus.* Some differences in the environment will therefore produce very marked effects on the developing organism.

On the other hand, organisms developing in the same environment may show marked differences, because they have inherited different characters. Two hen's eggs in an incubator, under the same conditions of temperature, moisture, etc., may develop birds, one with a rose comb and the other with a single comb, or one with white feathers and the other with brown. Obviously the environment is not a differential, but the difference was in the original eggs and is inherited from the previous generation. No one would suggest that even if the eggs were

* Stockard's result has since been shown to be due to differential destruction of the nerve plate in the embryo, the destruction beginning at the anterior end, as in Child's experiments with potassium cyanide.

incubated at different temperatures the single comb would be altered to a rose comb.

Clearly, then, some characters are produced by an environmental stimulus and others are determined by inheritance, although in both cases interaction of organism and environment takes place in the development of the character. A given character may occur in either or both categories. Thus fasciation or flattening of the stem in plants usually results from over-nutrition and is then, as a rule at least, not inherited at all. But in *Celosia cristata*, the coxcomb of gardens, extreme fasciation is a specific character, distinguishing this form from *C. plumosa*. Again, thickening of the epidermis or formation of corns results from friction of the skin of the hands or feet, and is not inherited. But keratosis is an inherited condition in which there is abnormal thickening of the skin without any excessive friction. Similarly it is now recognised that epilepsy may be a non-inherited modification produced perhaps by conditions at birth; or it may be germinal in origin, and so inherited.

When a new character appears through a variation, the first question one asks is whether it is inherited. It is impossible to determine this with certainty except by experiment—*i.e.*, by breeding from the new type. If it *is* inherited, one must conclude that a germinal change has taken place, leading to the production of a new character, or at least that a germinal rearrangement has taken place, making possible the appearance of the new character. If it is not inherited, then the conclusion is that a modification has been impressed on the organism by some feature of the environment.* The question to ask, then, is not whether heredity or environment is more important in the ontogeny of any character, but whether a difference (variation) which appears in an organism is due primarily to a difference in the environment or a difference in heredity (*cf.* Sumner, 1922).

This leads us to emphasise a point which is not always recognised—namely, that the relation between the organism and its environment is not the simple and direct relation between two reacting chemical substances—it is rather one of stimulus

* The possibility of the inheritance of acquired characters has not been considered here, because if it ever occurs in mankind it is probably too slow in its action to affect the practical problems of eugenics. The subject has been discussed from an evolutionary point of view elsewhere (Gates, 1921, chaps. viii.-xii.).

and response. It is, moreover, clear that not all elements of the environment are equally effective in modifying the organism. For example, a change in the light may have a striking effect on the development of one organism and no appreciable effect on another. The relations of an organism to its environment are therefore extremely complex, and can only be understood after elaborate analysis. But the higher organisms, and particularly man, have many regulatory mechanisms which enable him to triumph over extreme variations in the environment without being vitally affected by them. This, with his weapons and his intelligence, has enabled mankind to people the four corners of the earth in almost every extreme of climatic conditions where organisms can live at all. From a eugenic point of view it is to be remembered that while hereditary differences of all kinds are perpetuated in all conditions, yet optimum conditions are desirable for the full expression of the characters inherited by the organism. From this it follows that those who insist upon the importance of heredity in perpetuating good stocks should, at the same time, realise the desirability of creating an environment in which the best physical, mental, and moral qualities of the individuals can find free expression.

Before proceeding further it may be well to point out that whereas heredity was formerly defined or measured by the degree of resemblance between parents and offspring, this treatment of the subject will no longer suffice. Thus Brooks (1906) says: "So far as the word is used inductively in biology, heredity is the resemblance of child to parent, of offspring to ancestor, while the difference between parent and child is called variation." The study of alternative inheritance, which appears to be the most usual form of heredity, has made it necessary to revise such a definition of heredity, as well as our outlook with regard to its incidence. It has now become a commonplace of observation that the differences between organisms, as well as their resemblances, are often inherited. If a tall is crossed with a dwarf variety, we know that usually the second generation will inherit tallness and dwarfness—the parental differentiating characters—in a definite proportion, and that certain of the tall individuals will go on transmitting dwarfness. We may even cross two white varieties of plants or two albino animals, externally alike, and obtain coloured offspring. Yet we know that the colour in this case is not the result of variation. One of the necessary elements

in its production has been inherited from each parent, though neither possesses both. In such instances invisible (probably nuclear) differences have been inherited which, when combined, produce a striking externalised difference. Hence it is necessary, in speaking of inheritance, to recognise that both similarities and differences may be inherited, the one quite as truly as the other. Some of the differences, particularly the quantitative ones, which appear in offspring may, then, be the result of variation, germinal or otherwise; but many of them will be the result of inheritance.

LITERATURE

BROOKS, W. K. 1906. Heredity and variation: logical and biological. *Proc. Amer. Phil. Soc.*, xlv. 70-76.

GATES, R. R. 1921. Mutations and evolution. London: Wesley and Wheldon, pp. 118.

STOCKARD, C. R. 1909. The artificial production of Cyclopean monsters. *Journ. Exptl. Zool.*, vi.

SUMNER, F. B. 1922. Heredity, environment and responsibility. *Scripps Inst. for Biol. Research*, Bull. 10, pp. 12.

CHAPTER II

THE GENERAL ASPECTS OF HEREDITY IN MAN

Many vague conceptions of heredity were formerly held, and much ink was unprofitably spilled in an effort to explain or elucidate inheritance in the absence of adequate experiment. Human inheritance particularly has been the subject of innumerable crude, unscientific conceptions such as " failure " of inheritance when a particular trait does not appear in every generation, a belief in maternal impressions, or scepticism regarding the inheritance of mental traits. The scientific investigation of heredity may almost be said to have begun with Mendel's studies of single characters in garden peas, since the results of the early hybridisers were so contradictory and confused—owing partly to an unfortunate choice of material for crossing and partly to an unsuitable method of experiment—that they never led to a consistent point of view on which future progress could build. The rediscovery of Mendel's principle of segregation in 1900 therefore marked the beginning of an era in the study of heredity. It has become progressively clearer that while mass statistics of resemblances may furnish useful information where no other is available, yet such data cannot alone furnish a basis for an understanding of the hereditary process. The experimental analytical method is necessary here, as in other fields of biology. The results of the experimental method, however, can be and have been applied to genealogical pedigrees of inheritance in man with illuminating results. This method has, of course, certain definite limitations, since evidence is available only from such marriages as have taken place. But in many cases of simple Mendelian inheritance this evidence is quite as clear and unequivocal as though actual experimental crosses had been made for the purpose of determining the method of inheritance of particular traits.

The number of characters in man which are now known to follow a Mendelian type of inheritance is surprisingly large. It is therefore desirable to elucidate briefly the principles of Mendelian inheritance for those who are not already familiar with the matter. An elementary treatment of the subject

is to be found in Punnett's *Mendelism* and in many other books. While thus emphasising the importance of Mendelian heredity, particularly as regards the inheritance of abnormalities in man, we wish also to stress the value of biometric studies of inheritance, for there are many characters in which this is the only method of analysis which can be applied. The two methods are complementary and are becoming more and more closely interwoven in the study of heredity. On the one hand, experimentalists are recognising the advantages of a mathematical analysis of their results, while on the other, biometricians realise the advantages of material under experimental control. As it is now known that the same character may be quite differently inherited in different human pedigrees, it is important that biometricians should scrutinise every pedigree with great care, to avoid lumping together statistically things which may be really quite diverse although they refer to the inheritance of the same entity.

The interaction of both the experimental and the statistical method produces the ideal result, but this is, of course, not always possible. The view taken here is that while Mendelian heredity is very common in mankind, especially as regards the inheritance of abnormalities, yet it cannot be treated, at any rate for the present, as though it were universal in the human race. Many quantitative characters, and perhaps some racial characters, may be found not to follow simple laws of inheritance involving fixed germinal units.

As an example of Mendelian inheritance let us consider brachydactyly or short fingers in man, the digits having two joints instead of three. This condition is dominant to the normal, which is spoken of as recessive. Brachydactylous individuals have always married normals. Persons showing this trait have therefore always been the children of one normal and one abnormal parent. They are therefore hybrid or heterozygous in nature as regards this character, and, since they are brachydactylous in appearance, this condition is said to be dominant to the normal. Now the essential feature of Mendelian behaviour is that the factors or determiners for such a pair of characters as normal and brachydactylous fingers *separate* in the formation of the germ cells, so that half the germ cells of a brachydactylous person who had one normal parent will carry the factor for brachydactyly and half will carry the factor for normal fingers. If such a person marries a normal individual, all of whose germ cells are therefore carrying the

factor for normal fingers, then, on the average, half the children will be brachydactylous and half normal, for the chances for the germ cell matings—(1) normal × normal and (2) normal × brachydactyl—are equal. The result will be clear from the accompanying diagram (Fig. 1).

Hence we see that as long as matings of brachydactyls with normals continue, half the children will, on the average, be heterozygous brachydactyls (transmitting this character to

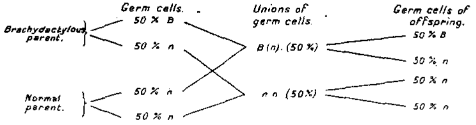

FIG. 1.—RESULT OF CROSS BETWEEN HETEROZYGOUS BRACHYDACTYL AND A NORMAL PARENT.

half their offspring), while the other half of the children will be pure normal, and transmit only the normal condition to all their offspring. In other words, the heterozygous dominants will continue to produce both types in equal numbers when mated to normals; while the normals derived from such a cross, being recessive, have entirely lost the brachydactylous con-

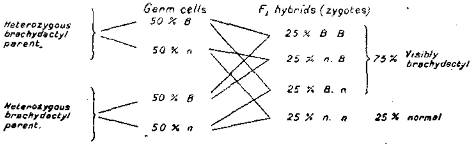

FIG. 2.—RESULTS OF CROSS BETWEEN TWO HETEROZYGOUS BRACHYDACTYL PARENTS.

dition (or rather never had it), and will therefore have only normal offspring even if two such normals from a brachydactylous cross mate together. For a full discussion of brachydactyly, see p. 145.

Many abnormalities in man are simple dominants and will therefore be inherited in the manner just explained.

In order to make clearer the nature of Mendelian heredity, let us consider the other types of mating which commonly

occur in organisms showing a single difference. If two such individual organisms which are pure or homozygous are crossed, the first hybrid generation (written briefly F_1) will show only the dominant character. But if two of these F_1 hybrids are intercrossed, their offspring will number on the average three dominants to one recessive. Thus, in a marriage between two heterozygous brachydactyls, three-fourths of the children would be expected to be brachydactylous. The reason for this will be understood from the above diagram (Fig. 2).

The four possible combinations of the two types of germ cells will occur with equal frequency, and since the factor for brachydactyly is absent from only one of the four combinations, it follows that only 25 per cent. of the offspring will be likely to have normal fingers. Of the other 75 per cent. which are brachydactylous, two out of three will be hetero-

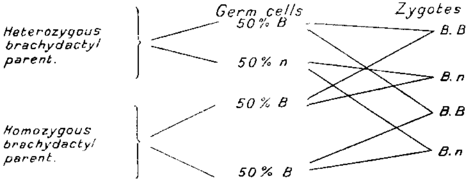

FIG. 3.—THEORETICAL RESULTS OF CROSS BETWEEN A HETEROZYGOUS AND A HOMOZYGOUS PARENT.

zygous (*i.e.*, with half their germ cells of each type), while one-third will be homozygous, carrying the determiner for brachydactyly in all their germ cells.

We may similarly consider the case where a heterozygous brachydactyl marries a homozygous brachydactyl.*

From the diagram (Fig. 3) it will be seen that the offspring from such a mating would be all brachydactylous, half of them heterozygous and half homozygous. So long as the former continued mating with homozygous brachydactyls the normal condition would be completely suppressed, and the strain would appear to be pure for brachydactyly. But if in any generation two heterozygous individuals mated, there would be one chance in four of the recessive condition reappearing. The

* There is some evidence that the homozygous brachyphalangous (related) condition is non-viable and therefore cannot exist (see p. 154).

sudden appearance of a reversion or throw-back in a pedigree strain, for example, of cattle, is often to be accounted for in this way. A recessive character may thus be carried in the germ plasm of a strain for many generations, only to crop out again when a chance mating of two individuals heterozygous for this character takes place.

It is not known how or when brachydactyly originated, but it probably occurred centuries ago, and presumably arose in the first instance as a mutation—*i.e.*, a sudden and probably spontaneous germinal change.*

Fortunately, the segregation which takes place in germ-cell formation can now be referred to definite elements in the cells—namely, the chromosomes. These are the elements of the nucleus whose constancy in number and shape for each species of animal and plant is one of the remarkable features of organic structure. In the complicated process of mitotic nuclear division, which happens whenever cells divide in the growth and development of the organism, the essential fact is that they are split lengthwise, so that each daughter cell contains in its nucleus the longitudinal halves of every chromosome. Although these bodies seem to merge in the resting nucleus into a mass in which the outlines of the separate chromosomes are lost, yet there are cases in which the outlines can still be traced, each chromosome forming a separate compartment or vesicle of the nucleus. There is also evidence that the parts of the various chromosomes maintain their special relationships throughout the period between one division and another even when visible boundaries are lost, or, at any rate, that they reassemble with the same arrangement as they disappeared. There is something, not at present understood, which maintains the unity of the chromosome as a persisting structure, and determines the constancy of its relative size and shape during mitosis in the various parts of the organism.

The organism begins its development from the union of the nuclei of egg and sperm. But when this union happens it is not a mere intermingling of two fluid substances, for the chromosomes, which are highly viscous in the condensed condition, maintain their separate identity; and in the subsequent nuclear divisions they frequently arrange themselves in pairs, each pair consisting of one chromosome of paternal origin (from the male germ cell) and one of maternal origin (from the female germ

* For a discussion of the causes and nature of mutation, see Gates (1915, chap. ix.).

cell). In many animals and plants the various pairs are distinguishable from each other in size or shape. The chromosomes may therefore be said to possess individuality and to show genetic continuity from generation to generation.

When the germ cells of an organism undergo maturation as the organism develops, the chromosome number in them is reduced to one-half. The essential feature of this complicated process is the separation of the pairs of chromosomes which are characteristic of the somatic nuclei, so that the nuclei of the eggs and sperms receive one member of each pair and hence have half as many chromosomes as the somatic cells.* Half the germ cells will thus receive one member of each pair, and half the other. This maturation process has been studied in great detail in hundreds of plants and animals, as well as in man (see p. 21). In the separation of pairs in the reduction divisions there is free assortment of the chromosomes. There are many reasons for believing that the chromosomes are the basis of Mendelian inheritance, and that the segregation of characters, which Mendel's experiments indicated took place in the formation of the germ cells, really depends on the separation of the chromosome-pairs in the reduction divisions. Indeed, the evidence is so manifold, and in certain experimental cases so conclusive, that few biologists longer question this conclusion.

That segregation of factors really takes place during meiosis (the period during which chromosome reduction occurs) has been shown by the formation of two types of pollen grain in certain hybrid rice plants. In these F_1 hybrids half the pollen grains contain starch grains, like the pollen grains of one parent, while the other half contain no starch. Fig. 4, from a section of an anther treated with iodine, shows the two types of pollen grains scattered in equal numbers through the anther.

Thus in an organism which is heterozygous for one pair of characters, say short hair (dominant) or long "Angora" hair (recessive) in guinea-pigs, the F_1 hybrid animals will have short hair, and all their cells will contain a pair of chromosomes which differ in that one chromosome contains the determiner for short coat, while its mate contains the determiner for long coat. When the germ cells of this guinea-pig are formed, this pair of chromosomes, like the other pairs, is separated, and half the eggs or sperms, as the case may be, get the chromosome

* Further complications of this process need not concern us here.

with the determiner for short hair, while the other half receive its mate containing the determiner for long hair. From this it follows, as shown in the diagram in Fig. 1 (p. 9), that three-quarters of the individuals in the next generation (F_2) will have short hair, the remaining quarter having Angora hair. This is because when the eggs and sperms unite in fertilisation, half the eggs and half the sperms will contain the chromosome determining short hair, while the other half carry its mate with the determiner for long hair. The fertilised eggs will then be

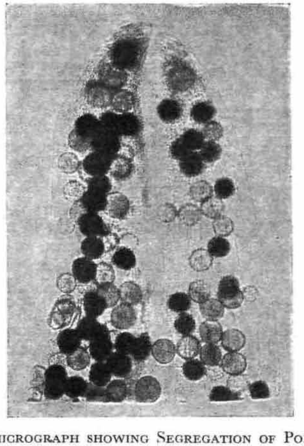

FIG. 4.—PHOTOMICROGRAPH SHOWING SEGREGATION OF POLLEN TYPES IN A RICE HYBRID. (After Parnell, 1921.)

of three types: (1) containing a pair of chromosomes, both of which carry the determiner for short coat. When these eggs develop into organisms which can be bred together, they can obviously give only short-coated offspring. They are homozygous dominants. (2) Some fertilised eggs will contain a pair of chromosomes with determiners respectively for long and short coat, and, according to the laws of chance combination, they will be twice as numerous as the last. They are the heterozygous dominants, their bodies indistinguishable from

the pure dominants (when dominance is complete), but their germ plasm as well as all their body cells containing an " unequal " pair of chromosomes which will separate as in the F_1 to produce the next generation. These two classes of F_2 animals, together making up three-quarters of the offspring, are visibly short-coated. (3) In the third class of fertilised eggs both chromosomes of this pair will contain the determiner for long coat. They will develop into long-coated animals, their body cells and germ cells will all contain the descendants of this pair of chromosomes, and they will give only long-coated offspring when bred together. They are the homozygous recessives, and because they result from chromosome recombinations taking place according to chance, they are as numerous as the first class, the homozygous dominants.

If D stands for any dominant character and R for the corresponding recessive, then the F_1 will be DR, and the F_2 generation from DR × DR will, as shown in the last paragraph, consist of the three types, DD, DR, and RR, in the ratio 1 : 2 : 1, as regards their germinal constitution. As regards their external or phenotypic appearance, however, there will be but two types, three individuals showing the dominant character to one the recessive. This is the famous 3 : 1 ratio.

There are several characteristic features of a dominant character in human pedigrees, as seen in the case of brachydactyly: (1) Individuals showing the character are usually heterozygous (DR); (2) they usually marry normals or individuals with the corresponding recessive character, and hence (3) half their children will show the dominant, since the mating is DR × RR. (4) The character will appear in every generation, one of the parents of each family or sibship in the line of descent showing it. These various features usually make any extensive pedigree of a dominant human character recognisable at once as dominant and not recessive. See, for example, Fig. 47, p. 160.

The history of the chromosomes in organisms was worked out quite independently of genetic experiments, but they furnish precisely the mechanism required to explain Mendelian behaviour, and the main facts of their history were known before the rediscovery of Mendel's laws in 1900. The number of freely assorting groups of Mendelian characters in a species should therefore be the same as the number of pairs of chromosomes; and the experimental work, particularly with the fruit fly *Drosophila* and the sweet pea, clearly indicates that this is

the case. In man, the number of chromosomes is a high one (48), and there should therefore be much free assortment of characters in inheritance, unless some special condition, such as linkage between chromosomes, exists (see p. 21).

Differences in the chromosomes in crossed races appear to determine the different types and combinations of characters which arise in the offspring. It thus appears that Mendelian differences in general have originated as mutations, probably through an alteration in a portion or locus of a chromosome. That the differences which arise in this way are inherited as Mendelian factors or genes results, then, from the manner of distribution of the chromosomes in the reduction divisions, when the nuclei of the germ cells are formed. Mutations seem to arise in the germ plasm at relatively infrequent intervals. In some cases the same mutation appears independently more

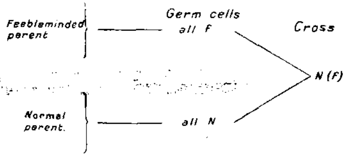

FIG. 5.—RESULT OF CROSS BETWEEN A DOMINANT AND A RECESSIVE CHARACTER IN F_1.

than once. They may then be handed down to later generations for an indefinite period. If the gene represents a dominant character, that character will be represented in every generation, but a recessive may be transmitted indefinitely in the germ plasm without coming to light until it meets a similar recessive from another strain. This sometimes happens in the marriage of relatives.

Let us now consider the inheritance of a recessive Mendelian character. Feeble-mindedness may be taken as an example, for it appears to be frequently inherited as a simple Mendelian recessive. Constructing a diagram (Fig. 5), we see that all the germ cells of a feeble-minded person will carry the factor for feeble-mindedness, since the character is recessive.

If mated with normal, the children will all be normal for the same reason, and the defect will seem to have disappeared. But these normals will all be heterozygous, carrying the defect for feeble-mindedness in half their germ cells. If two such

persons mate together, it will be seen from the following diagram (Fig. 6) that half the germ cells of each will be normal and half carry the defect.

This will give four combinations of germ cells occurring with equal frequency. Three of them, or on the average three-fourths of the offspring, will be normal, the other fourth will be feeble-minded. Moreover, of the normals two-thirds will be carrying feeble-mindedness as a recessive character, while the other third will be untainted. Further, it is clear that if the Mendelian behaviour is strictly adhered to, two feeble-minded parents can have only feeble-minded offspring. The exceptions to this rule, if they exist, are so few as to be negligible. For a further account of feeble-mindedness see p. 267.

There is no doubt that the germ plasm of any human strain contains numbers of invisible recessive characters, which may be transmitted for generations without appearing, until

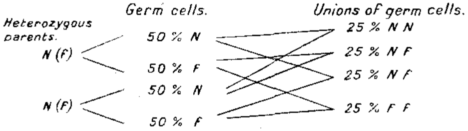

FIG. 6.—RESULTS OF ABOVE CROSS IN F_2.

union with an individual carrying the same recessive character may ultimately bring it out in some (25 per cent.) of the offspring. The presence of similar, undesirable recessive characters in the germ plasm is thus the chief danger from inbreeding or intermarriage of cousins. The main features of a recessive character are, then, that it disappears in the first generation of a cross between a pure dominant and a pure recessive, while it reappears in about one-quarter of the offspring of two individuals heterozygous for the character. It will appear in about half the offspring of matings between a heterozygous normal and a (pure) recessive.

Human pedigrees of a recessive character are thus very different from those of a dominant. (1) The character suddenly appears in about one-quarter of the children from a marriage in which neither parent shows the character. (2) It is apt to be sporadic in its occurrence in any pedigree. (3) It will not often occur in successive generations in the same line

of descent, but (4) if it does, both parents and all the children of the family will show it. See, for example, Fig. 24, p. 86.

Another type of Mendelian character, which in its inheritance follows exactly the distribution of the sex chromosomes, is known as sex-linked inheritance. Such characters evidently depend for their origin upon mutations occurring in the sex chromosomes. As an example of this in man we may consider colour-blindness. The nature of this inheritance-mechanism will be clear from the diagram (Fig. 7), showing the history of the sex chromosomes as they appear to behave in man.

The history of the sex chromosomes has been clearly shown in many animals, and in the fruit fly *Drosophila* a large number of sex-linked mutations, determined apparently by changes in loci of the X-chromosome, have been studied.

A brief account is first necessary of the sex chromosomes as they apparently exist in man. Although many observations

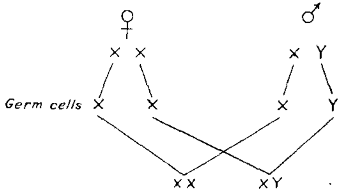

Fig. 7.—Diagram to show the History of the Sex Chromosomes.

have been made on the subject, the facts are not yet known with certainty; but the details are gradually becoming clear. It should first be pointed out that in many animals there is a recognisably unequal pair of chromosomes, XY, the X being large and the Y small. These sex chromosomes also differ in behaviour from the other chromosomes (autosomes), remaining in the condensed condition at certain stages of meiosis when the autosomes are loose and flocculent. The male animal contains XY in its body cells, and as these separate in meiosis, half the sperm contain X and half Y. All the eggs when ready for fertilisation contain X, since the female body cells are XX. In fertilisation, the XY and XX combinations will therefore produce males and females in equal numbers. In some animals, however, the Y has been lost and the X has no mate. Hence the males are XO and the females XX. Similar con-

ditions have been discovered in various diœcious plants. This chromosome mechanism maintains approximate equality in the numbers of the two sexes. But various conditions may disturb this equality, leading to preponderance of one sex in numbers.

At one time it appeared that the negro had 24 chromosomes and the white man 48, but the chromosomes in man as well as in other mammals (and in birds) are difficult to fix properly, and this apparent difference was probably due to clumping of the chromosome pairs in the process of fixation, so that they looked like single chromosomes. Also in the earlier accounts one or two more chromosomes were found in the female than in the male, but later investigators have found that there is a pair (XY) of sex chromosomes which are distinguishable by their shape and behaviour from the other chromosomes. It appeared from the studies of Guyer (1910, 1914) and of Montgomery (1912) on human spermatogenesis that the male negro possesses 22 chromosomes, including 2 sex or accessory chromosomes. Montgomery found that the accessories were irregularly distributed in the reduction divisions. It was inferred that the female number was 24. Von Winiwarter (1912), however, studying members of the white race, found 47 chromosomes in man and 48 in woman (oögonial divisions). Farmer, Moore and Walker (1906), in examining pathological tissue (somatic cells) presumably of white people, found usually 32 chromosomes, while Wieman (1913) counted 33 to 38 chromosomes in a human embryo the parentage of which is not stated. Rappeport (1922) counted the chromosomes in the epithelium of the pleura, peritoneum, and amnion from human embryos, finding 40-42, but being unable to decide whether the difference found belonged to different individuals or sexes. Wieman (1917) described human spermatogenesis with 24 chromosomes in both negro and white, including an XY pair of sex chromosomes which divide in the first reduction division and segregate in the second, unlike the other chromosomes which segregate in the first and divide in the second. Still more recently, Painter (1921), in an account of spermatogenesis in both whites and negroes from Texas, finds approximately 48 chromosomes in both, including an XY pair of sex chromosomes. This is a partial confirmation of von Winiwarter. It appeared at one time that all these investigators might be right in their determinations of numbers, and that human individuals might exist with 24 ($2n$ or diploid), about

36 ($3n$ or triploid), and 48 ($4n$ or tetraploid) chromosome numbers. The chromosomes of all mammals are, however, notoriously difficult to deal with, and it now appears that clumping gave rise to a false appearance of different numbers.

From the more recent work it is agreed by von Winiwarter (1912), Painter (1923), Oguma and Kihara (1923), and Winiwarter and Oguma (1925, 1926), that the diploid chromosome number in man, including the white, black, and yellow races, is 48. There is still, however, difference of opinion as to whether the chromosomes are an XY pair, in which case both sexes would have the same number, or whether the X has no mate, in which case the male chromosome number would be 47. From the appended list of recent chromosome counts in mammals (Table I.) it will be seen that von Winiwarter finds the XO arrangement not only in man but also in the cat, while Painter and others find an XY pair in many cases. The XY pair are found to be markedly smaller than the autosomes, the Y in man being very small, and in certain marsupials extremely minute according to work of Agar and Greenwood. There is much evidence from the spermatogenesis of insects and other animals that the Y chromosome is on the verge of extinction in some species and has been extinguished or at least passed below the limits of visibility in others. But no case is known in which some males of a species retain the Y while others have lost it. Winiwarter and Oguma suggest (1926) that this may actually be the case in man, but this seems scarcely probable. Further investigations will no doubt clear up this point.

Closely connected with the question of an XY or XO sex-chromosome mechanism in man is the variation in size of the sperm. Parkes (1923) has obtained some evidence, from measurements of head-lengths of the spermatozoa in man, that they fall into a bimodal curve, which would correspond with the male-producing and female-producing types. He has shown the same for the rat and mouse, but for the cat the evidence is uncertain.* Similar results had previously been obtained for the horse, the bull, and the dog. Dimorphism of the sperm may quite probably play a part in determining the sex ratio at conception. The male-producing sperm, whether they have a Y (which is always smaller than the X) or no Y

* As these conclusions are not founded on very large numbers of measurements they require confirmation before being accepted as proven.

at all, would be lighter, probably travel faster, and perhaps account for the well-known excess of males at birth.

Turning again to Table I., it shows some interesting features bearing on chromosome numbers and relationships in the mammals. In the first place it will be seen that one of the Old World monkeys has 48 chromosomes, the same number as in man. This number, a relatively high one, can then probably be taken as the characteristic number for the Primates. On the other hand, one of the New World monkeys has a higher number.

Surveying the table as a whole, we see that chromosome numbers have increased during the evolution of the mammals. The marsupials begin with 12 or 14 and go to 22, although some of these numbers may of course still require revision. In the Eutheria the numbers progress from 36 to 60, or even 78 in one study of the dog. Forty-eight, which appears in the Insectivora and Cheiroptera as well as man and a monkey, is probably the primitive number for the Primates. As these numbers are extended and corrected, the interest in this comparative study will increase.

The study of chromosomes and phylogeny has become of great interest in plants, where chromosome numbers often run in multiples in the species of a genus (see Gates, 1924). But there appears to be very little polyploidy in animals, possibly because they are usually bisexual and not hermaphrodite. Much has yet to be learned of the ways in which specific chromosome numbers undergo phylogenetic change. In the mixed strain of hybrid rats studied by Dr. Swezy (1927), she found 21 rats with 42 chromosomes and 17 with 62 chromosomes. How the higher number of chromosomes arose is unkown, but in crosses between animals having these numbers the offspring again had 42 or 62. This indicates that the only viable combinations of germ cells were 21+21 or 31+31. Dr. Swezy (1928) has since found that although the number of chromosomes in four wild grey rats was $2n=42$, yet some of their secondary spermatocytes had 21 chromosomes and some 31, the same dimorphic condition of the sperm being found in two further colonies of white rats. She suggests that 42 is the basic number in *R. novegicus* and that the sperm dimorphism is leading towards a new stable species with $2n=62$ chromosomes.

Evans and Swezy (1928) have recently studied the chromosomes in both adult and embryonic somatic tissues of human

TABLE I

RECENT CHROMOSOME COUNTS IN MAMMALS AND MAN

Primates.	*Chromosome Number.*	*Sex Chromosomes.*	*Author.*
Man, white	47, 48	XO	Winiwarter, 1912.
	47, 48	XO	Winiwarter and Oguma, 1926.
	48	XY	Painter, 1923.
„ negro	48	XY	„ „
„ Japanese	47, 48	XO	Oguma and Kihara, 1923.
Rhesus macacus	48	XY	Painter, 1924.
Brown Cebus Monkey ..	54	XY	„ „
EUTHERIA:			
Cheiroptera—House bat ..	48	—	„ 1925.
Insectivora—Hedgehog ..	48	—	„ „
Ungulata—Pig	40	—	Hance, 1917.
Horse	60	XY	Painter, 1924.
Cattle	±60	—	Krallinger, 1927.
Edentata—Armadillo ..	60	—	Painter, 1925.
Rodentia—Rabbit	44	XY	„ 1926.
Mus wagneri albula ..	40	XY	Minouchi, 1928.
Albino rat	37, 38	XO	Allen, 1918.
„ „	42	XY	Evans and Swezy, 1928.
Black rat (*Rattus Rattus*)	40	XY	Pincus, 1927.
Norway rat (*R. norvegicus*)	42	XY	„ „
Mixed strain, Norway × albino rat	42, 62	—	Swezy, 1927.
Mus norvegicus albus ..	42	XY	Minouchi, 1928.
House mouse	40	XY	Cox, 1926.
„ „	39, 40	XO	Yocum, 1917.
Carnivora—Dog	50+	—	Painter, 1925.
„	78	XY	Minouchi, 1928.
Cat	35, 36	XO	Winiwarter, 1920.
	38	XY	Minouchi, 1928.
MARSUPIALS:			
Didelphys virginiana	22	XY	Painter, 1922, 1924; Hoy and George, 1929.
Dasyurus maculatus	14	XY	Greenwood, 1923.
Sarcophilus ursinus	14	XY	„ „
Macropus ualabatus	12	XY	Agar, 1923.
Potorous tridactylus	12	—	Ellery, 1925.
Phascolomys mitchelii ..	14	—	Altmann, 1925.
Phascolarctus cinereus ..	16	—	Greenwood, 1923.
Pseudochirus peregrinus ..	20	—	Altmann, 1925.
Trichosurus vulpecula ..	20	—	„ „
Petauroides volans	22	XY	Agar, 1923.

males and females. They find that in males the autosomes are consistently longer than the corresponding ones in females, the longest pair of autosomes in the male being longer than the longest pair in the female. A similar difference is found in the somatic cells of male and female rats. It is suggested that this difference may be related to the larger average size of males than females, and that the difference in autosome size probably appears at fertilisation and is a secondary sexual character impressed on the cells throughout development by the presence of the X or the Y chromosome. It would be instructive in this connection to measure the comparative size of the cells in various tissues of males and females, both in man and in other animals. Evans and Swezy also find the chromosome sizes more variable in males than females, which is in harmony with the believed greater variability of men than women.

We are now in a position to understand the mechanism of inheritance of sex-linked characters, such as colour-blindness and hæmophilia, in man.

The diagram (Fig. 8) shows only the sex chromosomes, which are taken to be XX in the female and XY in the male.

The underlined $\underline{X}$ is carrying the factor for colour-blindness. The male, $\underline{X}$Y, would therefore be colour-blind. Mated with a normal woman, their male children would all be normal. The $\underline{X}$ chromosome of the father, however, goes to all his daughters, who are all, therefore, transmitters of the defect to future generations. Married to a husband who is normal, they will transmit the defect to half their children of both sexes, as shown in the next two lines of the diagram. Only the sons will be colour-blind, however, while the daughters will all be heterozygous for the condition but will have normal sight. Hence normal may be regarded as dominant to the colour-blind gene.

The last three lines of Fig. 8 show how a colour-blind father and a heterozygous mother will have a family in which half the daughters show the defect and half the sons will show it.* If the mother were homozygous for colour-blindness and the father also carried it, then all the children would be colour-blind. There is no instance of a colour-blind father transmitting the condition visibly to the next generation, except in

* There are some irregular cases in which colour-blindness shows in a heterozygous woman. In such a case the dominance of the normal condition is incomplete.

connection with a mother who transmits it. This criss-cross type of inheritance is more complicated than simple Mendelian behaviour in which both parents take the same part in inheritance, but it is simply explained by assuming that the colour-blind condition follows the path of the defective X chromosome

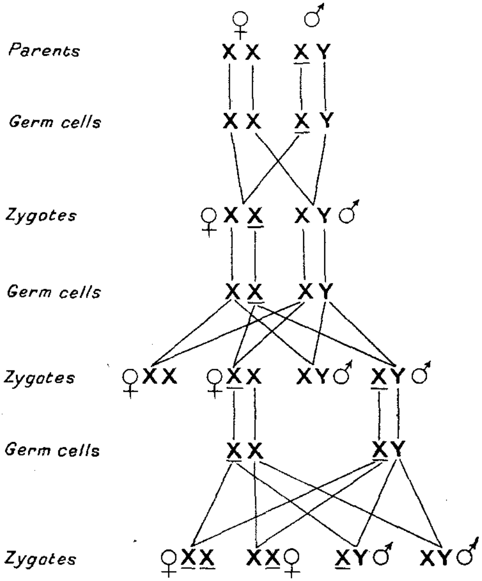

FIG. 8.—DIAGRAM TO ILLUSTRATE THE INHERITANCE OF SEX-LINKED CHARACTERS THROUGH THE X-CHROMOSOME.

from generation to generation. Thus the chromosomes offer a complete explanation of a very complicated form of hereditary behaviour. If such a chromosome mechanism were unknown, the cause of such behaviour on the part of sex-linked characters would be a complete mystery.

Pedigrees of such sex-linked characters thus have several

peculiarities (see Fig. 21, p. 82). (1) The transmission is from an affected father through his daughters, all of whom should be carriers (since they all get an X chromosome from their father), to half their sons (those which get the X chromosome carrying the defect). (2) Usually only males will show the condition, at least fully. (3) It will appear in males of alternate generations. (4) An affected man married to a heterozygous (carrier) woman may produce homozygous daughters who show the condition and will transmit it to *all* their sons, while all their daughters will be heterozygous carriers. Other types of sex-linked inheritance will be referred to later.

It appears, then, that in all these cases the fact that the differences are inherited as Mendelian factors results from the manner of distribution of the chromosomes in the reduction divisions at the time the germ cells of the organism are matured. It may be that some of the fundamental *resemblances* between related organisms are inherited in a different way. Since in experimental breeding it is only possible to study directly the inheritanee of differences, evidence concerning the process of inheritance of resemblances must necessarily be indirect and closely wrapped up with development itself.

We may now consider some of the differences appearing in man which so often follow one of these types of Mendelian behaviour. While dominance is very common, especially in connection with abnormalities, it is not by any means universal. There is, for instance, no dominance in such a character as skin colour, but the first generation is intermediate and back-crosses will further dilute the colour. It is probable that in organisms at large complete dominance is the exception rather than the rule. Why dominant mutations should be so numerous in man is at present quite unexplained. In *Drosophila*, only about a dozen dominant mutations have appeared among some 300, all the rest being recessive, and they are equally uncommon in other organisms.

The biological characters or differences observable in the human race and for the most part inherited include not merely the more striking racial divergencies, but also the innumerable structural and mental or temperamental differences that we see in the individuals of any population, however " pure " the race. Colour of hair and eyes, height and size of various parts of the body (for there is some evidence that these may be independently inherited for different segments), conformation

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of the head and features, size and shape of eyes, ears, nose, mouth, hands, and feet—there is good reason to believe that the element of inheritance enters into the perpetuation of a host of such differences as well as others more minute. Everyone can cite, from his own experience, cases of such essentially physiological traits as longevity and early baldness or greyness "running in families."

A large body of detailed evidence concerning heredity in man has accumulated in recent years. It is not my purpose to attempt anything like a complete citation of this work, but we may enumerate the more important studies which have been made on this subject, and some of the conclusions which have been reached; for our knowledge of the inheritance both of normal and abnormal traits in man must always form the chief basis for eugenic action.

To write a general introduction to genetics would unduly enlarge the size of this book. The reader is therefore referred to such works as Punnett's *Mendelism*, which is a simple introductory account, *Mendel's Principles of Heredity*, by Bateson, and *The Theory of the Gene*, by Morgan, for the main facts of heredity in plants and animals. It is necessary, however, in concluding this chapter, to explain certain terms which will frequently be used in this volume.

An organism is homozygous or pure for any character when both the germ cells which united to form the organism contain a determiner, factor, or gene (these terms are essentially interchangeable) for that character. It is heterozygous or hybrid for that character when one parent germ cell contained the determiner and the other did not. A heterozygous organism is therefore in a condition of germinal unbalance as regards each factor which is represented but once (not twice) in its germ plasm. Any organism may of course be homozygous for some factors and heterozygous for others. The particular factor for which an organism is homozygous will be represented in all its germ cells, while the factor for which an organism is heterozygous will only be present in half its germ cells.

The characters or factors which form an alternative pair in inheritance are spoken of as *allelomorphs*. Thus brachydactylous and normal fingers are an allelomorphic pair of characters. Blue eyes and brown eyes may also be a pair of allelomorphs.

The terms *genotype* and *phenotype* were introduced to distinguish between the germinal composition of any organism and its external appearance. In an entirely homozygous

organism the two will correspond, but if an organism carries recessive factors in its germ plasm its germinal constitution or genotype will differ from its appearance or phenotype. Also there are cases where two or more factors combine to produce a single phenotypic character. Again, in cases of partial or variable dominance the phenotypic appearance may not always correspond with the genotypic constitution.

The numerous abnormalities in man the inheritance of which has been studied are usually based upon a single factor, which is most frequently dominant but in many cases is recessive, and in some is sex-linked. The only satisfactory explanation of sex-linked abnormalities, such as colour-blindness, which have nothing to do with sex, is that they are determined by a gene carried in a sex chromosome. In the same way, ordinary non-sex-linked dominant or recessive characters are determined by factors carried in the ordinary chromosomes or autosomes. A fact which has been more strikingly exemplified in man than in plants or animals is that the same abnormality may be inherited in quite different ways in different pedigrees. Thus microphthalmia is a dominant in some pedigrees, a recessive in others, and sex-linked in still others (see p. 101). The presence or absence of sex-linkage is, as we have already explained, due to the location of thc controlling gene in a particular part of the germ plasm—*i.e.*, in a sex chromosome; but why the same character should be inherited as a dominant in the germ plasm of one family and as a recessive in another is not at present clear. Usually the condition of dominance or recessiveness is quite constant in any pedigree; but occasionally dominance is variable or even alternating, and cases are recorded both in animals and in man where a character at first recessive has become dominant in later generations. These require further analysis.

It must here be pointed out also that there are different forms of sex-linked inheritance. These will be discussed as the cases arise later, but we may refer here to a useful classification of different types of sex-linked inheritance in man by Enriques (1922, 1928). He recognises four types:

1. Diagynic heredity, through the X chromosome. Colour-blindness and hæmophilia are of this type, which has already been explained on p. 22. It has also been called male-sex-linked inheritance, or the condition has been described as dominant in the male and recessive in the female.

2. Holandric heredity, through the Y chromosome. This is confined to the male line, never appearing in females or being

transmitted by them. It is sometimes spoken of as a male-to-male descent or one-sided male inheritance. Certain pedigrees of syndactyly appear to show this type of inheritance, but there is still some doubt (see p. 19) as to whether the sex chromosomes of man are of the XY or the XO type. Inheritance of this type occurs commonly in the millions fish, *Lebistes*.

3. Diandric heredity is not known in man, but occurs in animals such as the moths, where the female is the heterozygous or heterogametic sex.

4. Hologynic heredity is confined to the females in a pedigree (see, *e.g.*, Fig. 22, p. 84), and must be inherited through the X-chromosome. The explanation of such pedigrees in man, where the male is the heterogametic sex, is not clear. But in the killifish, *Platypœcilus*, where the female is heterogametic, such one-sided feminine inheritance or female-to-female descent has recently been described by Fraser and Gordon (1928), resulting from crossing-over between the sex chromosomes.

The terms diagynic, holandric, and hologynic are thus convenient for describing certain definite types of inheritance in man.

5. In certain human pedigrees (see dipsomania, p. 275) the inheritance is sex-limited, dominant in males and recessive in females, like the horns in certain breeds of sheep.

Since the number of chromosomes in man is high (24 pairs) it is to be expected that free assortment will usually be found between a particular character and any others which happen to be present in the same pedigree. But indications of more or less complete linkage between certain characters in man are not wanting. Thus everyone knows that dark hair and dark eyes or light hair and light eyes usually go together, although exceptions occur—*i.e.*, individuals with dark hair and light eyes or light hair and dark eyes. Theoretically it might be supposed that, *e.g.*, the factor for blue eyes was linked with the factor for hexadactyly or any other unrelated condition, the hexadactylous individuals in a pedigree having usually blue eyes, while the five-fingered members had usually brown eyes. Very little is known of such cases in ordinary human pedigrees at the present time, although in interracial crosses linkage of characters frequently occurs. Linkages of the kind above mentioned, when they occur, as they frequently do, in plant and animal experiments, are explained by the hypothesis that the genes for the two linked characters are carried in the

same chromosome. In *Drosophila melanogaster*, the fruit fly which has four pairs of chromosomes, the hundreds of known mutations all fall into four linkage groups, one of which is sex-linked; and in the sweet pea, which has seven pairs of chromosomes, the nineteen known Mendelian factors all fall into seven linkage groups. Hence we may expect to find in man twenty-four independent linkage groups, the characters in one group being linked with sex. We do find in man that various eye or hand abnormalities may occur together in the same pedigree, but this is a different thing, the explanation of which is not yet clear. It appears to be in some families merely a tendency to accumulate defects through mate selection, and not due to any germinal linkage between the conditions involved.

When linkage is incomplete we get "crossing-over." If Aa are one pair of allelomorphs and Bb another pair, and if a man having say two dominant abnormalities, A and B, marries a normal woman (ab), then if A and B are linked the later generations will mostly show AB or the corresponding normal condition ab. But if the linkage is incomplete, then a certain number of "cross-overs," AB and ab, will appear, while if there is no linkage at all, Ab and aB will be as frequent as AB or ab. Now an immense amount of breeding work with Drosophila has shown that the amount of crossing-over between any two pairs of linked factors is relatively fixed, and this is believed to result from the genes or factors each occupying a fixed position in a particular chromosome or its mate. There are recent indications of crossing-over in the blood groups (see p. 197), and this may be regarded as the first likely case of the kind in man. The higher the number of chromosome pairs in an organism, the more infrequent should be the observed cases of crossing-over, but no doubt it will be found as a further development in the study of human heredity. Cases are also known now, in both plants and animals, in which the degree of crossing-over differs in the two sexes.

Multiple allelomorphs must also be mentioned. If any new germinal condition can arise through a mutation resulting from a change in a locus of a chromosome, then there is reason to suppose that the same locus can undergo a different change. Thus we would have three conditions, the original as well as two derived conditions or mutations. These commonly affect the same organs and usually represent different degrees of the same change. In Drosophila there is a series of several allelomorphs, all affecting eye-colour and all shown by breeding

experiments to have resulted from a mutation in the same locus of the "same" chromosome. In man it is possible that some of the eye colours between brown and blue belong to such a series of multiple allelomorphs.

Multiple factors are different, in that while they affect the same character they lie in different pairs of chromosomes. In the case of multiple allelomorphs, no more than two can ever be present in the same individual—one in each member of a particular pair of chromosomes. This is Bernstein's theory of the human blood groups (see p. 192). But with multiple factors, cases are known in cereals where the same factor is represented three times or more. These factors may be cumulative in effect, each intensifying for instance the colour of the seed or glume, or there may be no such intensifying effect. In the well-known case of hooded rats there is a series of spotting factors, each of which extends further the colour pattern of the coat. When the effects of the multiple factors are not cumulative, then in crosses involving two multiple factors the F_2 ratio will be 15 : 1 instead of 3 : 1, since only once in 16 will both factors be absent; and when three factors are involved the ratio will be 63 : 1. Interracial crosses in man appear to show the presence of multiple factors for skin colour, at least in the darker races.

Modifying factors are also of common occurrence in genetical experiments. They produce some minor modifying effect on the character for which another factor is mainly responsible. Cases are also known in which the co-operation of two or more unlike factors is required to produce a particular external character, and instances of this kind apparently occur in man. Probably cystinuria is one of them.

The term *parentela* has been introduced by van Bemmelen (1927) to denote all the descendants from a particular couple, and is useful in certain connections.

Lethal factors have become important in genetical literature. In plants, gametic lethals are known, in the presence of which the gamete fails to function, as well as zygotic lethals. In animals no gametic lethal has yet been discovered. It would lead to half the sperm or half the egg cells being non-viable. Zygotic lethals are usually non-viable in the homozygous but not in the heterozygous state. The gene for yellow coat colour in mice is a very good example of a zygotic lethal, the yellow mouse being viable only in the heterozygous state. In crosses between heterozygous yellow mice, ratios of 2 yellow : 1 grey

instead of 3 : 1 were obtained, which led to the conclusion that pure yellow mice were non-viable. The degeneration of certain of the young embryos in an early stage of development, when two mice heterozygous for yellow coat are bred together, was then looked for and such embryos were actually observed. Mohr (1926) has considered the cases of lethal factors known in domestic animals and man, but certain others, some of them more recently described, may be referred to here. Several cases of suggested lethals in man are considered in the appropriate places in this book.

Yamane (1925, 1927) describes a malformation of the colon in the horse, which is sub-lethal in the homozygous state. This factor produces complete atresia of the colon. The large intestine is entirely cut off from functioning, and death usually takes place two to four days after birth. This condition is often accompanied by glioma cerebri. It was found to have been introduced from Ohio into Japan forty years ago, through a Percheron stallion. This gene has now spread in horses all over Hokkaido. The same identical condition was found in the offspring of a stallion in Altmark, Germany.

Roberts (1926) described a sub-lethal deformity in new-born lambs in England. The limbs, especially the forelimbs, are contracted and perfectly rigid, so it is impossible to bend them. These lambs are almost always born dead. The condition is a simple Mendelian recessive in inheritance and is widely distributed in various flocks throughout England. It requires great care and much time to breed out successfully such a recessive lethal condition. In further observations, Roberts (1929) has found this condition not only in a flock of Welsh mountain sheep, but also in a Down breed, a Longwool breed and another Mountain breed.

Wriedt and Mohr (1928) have recently described a new recessive lethal mutation known as "amputated" in Swedish Holstein-Friesian cattle. It occurred in the same herd in which they described another recessive lethal mutation called hairless (*q.v.*). This breed of cattle is remarkable for the number of recessive lethal factors they are known to carry in their germ plasm. The "amputated" mutation was at first supposed to be the same as the "bulldog" type, but proved to be entirely different. It is called *acroteriasis congenita,* and is characterised by the absence of the feet and lower legs, atrophy of the maxilla, cleft palate and vestigial mandible, accompanied by hydrocephalus and other abnormalities. These calves die immediately after

birth. Heterozygous bulls × daughters of heterozygous bulls gave 102 normal : 13 abnormal, where expectation is 7 : 1. In another Swedish herd 23 more cases occurred. By tracing back pedigrees, it was found that this gene was introduced into Sweden about 1892 by the bull *Gallus M.* from Ostfriesland, Germany, and is now widespread in the breed, as is also the sub-lethal hairless. What is regarded as the best breeding practice has been followed with Holstein-Friesians, but in the presence of several recessive lethal factors these methods must be changed to prevent their recurrence. If bulls are tested to their daughters before breeding them for stock, it will soon be discovered if they are carrying any recessive factors.

LITERATURE

AGAR, W. E. 1923. The male meiotic phase in two genera of Marsupials. (*Macropus* and *Petauroides.*) *Quart. Journ. Micro. Sci.*, lxvii. 183-200 pls. 3.

ALLEN, E. 1918. Studies on cell division in the albino rat. *Journ. Morph.*, xxxi.

ALTMANN, S. C. A., and ELLERY, M. E. W. 1925. The chromosomes of four species of Marsupials. *Quart. Journ. Micro. Sci.*, lxix. 463-469, pls. 2.

VAN BEMMELEN, J. F. 1927. Heredity of mental faculties. *Proc. Konink. Akad. Wetens. Amsterdam.*, xxx. 769-795.

COX, E. K. 1926. The chromosomes of the house mouse. *Journ. Morph. and Physiol.*, xliii. 45-54, pls. 2.

ENRIQUES, P. 1922. Hologenic heredity. *Genetics*, vii. 583-589.

ENRIQUES. P. 1928. Le diverse forme di eredità "legata col sesso" nella specie umana, e la loro spiegazione. *Verh. V. Internat. Kongr. Vererb.*, i. 631-634.

EVANS, HERBERT M., and SWEZY, OLIVE. 1928. A sex difference in chromosome lengths in the Mammalia. *Genetics*, xiii. 532-543.

FRASER, A. C., and GORDON, M. 1928. Crossing-over between the W and Z chromosomes of the Killifish *Platypœcilus*. *Science*, lxvii. 470.

GATES, R. R. 1915. The modification of characters by crossing. *Amer. Nat.*, xlix. 562-569.

GATES, R. R. 1924. Polyploidy. *Brit. Journ. Exptl. Biol.*, i. 153-182.

GREENWOOD, A. W. 1923. Marsupial spermatogenesis. *Quart. Journ. Micro. Sci.*, lxvii. 203-216, pls. 2.

GUYER, M. F. 1910. Accessory chromosomes in man. *Biol. Bull.*, xix. 219-234, pl. 1.

GUYER, M. F. 1914. Accessory chromosomes in man. *Science*, xxxix.

HANCE, ROBERT T. 1917. The diploid chromosome complexes of the pig (*Sus scrofa*), and their variations. *Journ. Morph.*, xxx. 155-222, pls. 10, figs. 5.

HOY, W., E., JR., and GEORGE, W. C. 1929. The somatic chromosomes of the opossum (*Didelphis virginiana*). *Journ. Morph.*, xlvii. 201-225.

KRALLINGER, H. F. 1927. Die Chromosomen der Haustiere. *Zuchtungskunde*, ii. 441-466.

MINOUCHI, O. 1928. The spermatogenesis of the dog, with special reference to meiosis. *Japanese Journ. Zool.*, i. 255-268, pl. 1.
MINOUCHI, O. 1928. On the chromosomes of the domestic mouse (*Mus wagneri albula*). *Japanese Journ. Zool.*, i. 269-273, pl. 1.
MINOUCHI, O. 1928. On the chromosomes of the cat. *Proc. Imp. Acad. Tokyo*, iv. 128-130, figs. 4.
MINOUCHI, O. 1928. Spermatogenesis of the albino rat (*Mus norvegicus albus*). *Japanese Journ. Zool.*, i. 235-254, pls. 2.
MOHR, O. L. 1925. Bemerkungen über das Verhalten gametischer Letalfaktoren bei Tieren und bei Pflanzen. *Norske Vidensk. Akad. Oslo*, No. 5, p. 8.
MOHR, O. L. 1926. Über Letalfaktoren, mit Berücksichtigung ihres Verhaltens bei Haustieren und beim Menschen. *Zeits. f. Abst. Vererb.*, xli. 59-109.
MOHR, O. L. and WRIEDT, CHR. 1928. Hairless, a new recessive lethal in cattle. *Journ. Genetics*, xix. 315-336, pls. 2.
MONTGOMERY, T. H. 1912. Human spermatogenesis. *Journ. Acad. Sci. Phila.*, xv.
OGUMA, K., and KIHARA, H. 1923. Étude des chromosomes chez l'homme. *Arch. de Biol.*, xxxiii. 493-514, pls. 3.
PAINTER, T. S. 1921. The Y-chromosome in mammals. *Science*, liii. 503-504.
PAINTER, T. S. 1922. Studies in mammalian spermatogenesis. I. Spermatogenesis of the opossum (*Didelphis virginiana*). *Journ. Exper. Zool.*, xxxv. 13-45, pls. 3, figs. 8.
PAINTER, T. S. 1923. II. The spermatogenesis of man. *Journ. Exper. Zool.*, xxxvii. 291-334, pls. 6, figs. 4.
PAINTER, T. S. 1924. III. The fate of the chromatin-nucleolus in the opossum. *Journ. Exper. Zool.*, xxxix. 187-220, pls. 4.
PAINTER, T. S. 1924. IV. The sex chromosomes of monkeys. *Journ. Exper. Zool.*, xxxix. 433-460, pls. 5, fig. 1.
PAINTER, T. S. 1924. V. The chromosomes of the horse. *Journ. Exper. Zool.*, xxxix. 229-247, pls. 2.
PAINTER, T. S. 1924. The sex chromosomes of man. *Amer. Nat.*, lviii. 506-524, figs. 22.
PAINTER, T. S. 1925. A comparative study of the chromosomes of mammals. *Amer. Nat.*, lix. 385-409, pl. 1, figs. 8.
PAINTER, T. S. 1926. VI. The chromosomes of the rabbit. *Journ. Morph. and Physiol.*, xliii. 1-22, pls. 8, fig. 1.
PAINTER, T. S. 1928. A comparison of the chromosomes of the rat and mouse with reference to the question of chromosome homology in mammals. *Genetics*, xiii. 180-189, figs. 9.
PARKES, A. S. 1923. Head-length dimorphism of mammalian spermatozoa. *Quart. Journ. Micro. Sci.*, lxvii. 617-625, figs. 3.
PARNELL, F. R. 1921. Note on the detection of segregation by examination of the pollen of rice. *Journ. Genetics*, xi. 209-212, pl. 1.
PINCUS, G. 1927. A comparative study of the chromosomes of the Norway rat (*Rattus norvegicus* Erxl.) and the black rat (*Rattus rattus* L.). *Journ. Morph. and Physiol.*, xliv. 515-538, pls. 4.
RAPPEPORT, TH. 1922. Über die somatische Mitose des Menschen. *Arch. f. Zellforsch.*, xvi. 371-382, pl. 1, figs. 2.
ROBERTS, J. A. F. 1926. A hereditary lethal deformity in new-born lambs. *Journ. Min. Agric.*, 795-801, pl. 1.

ROBERTS, J. A. F. 1929. The inheritance of a lethal muscle contracture in the sheep. *Journ. Genetics*, xxi. 57-69, pl. 1.
SWEZY, OLIVE. 1927. The chromosomes of the rat. *Science*, lxvi. 601-602, figs. 3.
WIEMAN, H. L. 1913. Chromosomes in man. *Amer. Journ. Anat.*, xiv 461-471, figs. 10.
WIEMAN, H. L. 1917. The chromosomes of human spermatocytes. *Amer. Journ. Anat.*, xxi. 1-21, pls. 4.
WINIWARTER, H. 1912. Études sur la spermatogenèse humaine. I. Cellule de Sertoli. II. Heterochromosome et mitoses de l'epithelium séminal. *Arch. de Biol.*, xxvii. 91-189, pls. 2.
WINIWARTER, H. 1920. Les mitoses de l'epithelium du chat. *Arch. de Biol.*, xxx. 1-87, pl. 1.
WINIWARTER, H., and OGUMA, K. 1925. Recherches sur quelques points controversée de la spermatogenèse humaine. *C. R. Assoc. des Anat.* pp. 7, figs. 4.
WINIWARTER, H. and OGUMA, K. 1926. Nouvelles recherches sur la spermatogenèse humaine. *Arch. de Biol.*, xxxvi. 99-166, pls. 2.
WRIEDT, CHR., and MOHR, O. L. 1928. Amputated, a recessive lethal in cattle; with a discussion on the bearing of lethal factors on the principles of live stock breeding. *Journ. Genetics*, xx. 187-215, figs. 3.
YAMANE, J. 1925. The lethal malformation of the colon in the horse. *Trans. Congress Far East Assoc. Trop. Med.*, Tokyo, pp. 815-818.
YAMANE, J. 1927. Über die *Atresia coli*, eine letale, erbliche Darmmissbildung beim Pferde, und ihre Kombination mit Gehirngliomen. *Zeits. f. Abst. u. Vererb.*, xlvi. 188-207.
YOCUM, B. 1917. Some phases of spermatogenesis in the mouse. *Univ. Cal. Publ. Zool.*, xvi. 371-380.

CHAPTER III

INHERITANCE OF STATURE

Two of the earliest subjects studied in connection with human heredity were naturally enough stature and eye-colour. Galton dealt with these traits in his *Natural Inheritance*. I have pointed out elsewhere (1914) that Galton was a believer both in continuity and discontinuity in variation, and also in alternative as well as blended inheritance. His point of view with regard to the inheritance of these two characters may be well illustrated by a quotation from *Natural Inheritance* (p. 138) : " Stature and eye-colour are not different as qualities, but they are more contrasted in hereditary behaviour than perhaps any other common qualities. Parents of different statures usually transmit a blended heritage to their children, but parents of different eye-colour usually transmit an alternative heritage." He also remarks (p. 139) : " The blending in stature is due to its being the aggregate of the quasi-independent inheritance of many separate parts, while eye-colour appears to be much less various in its origin." Instead of Galton's conception of particulate inheritance, we now think in terms of such abstractions as multiple allelomorphs or multiple factors. But this conclusion of his concerning stature has been supported by Davenport (1917), who concludes from a considerable aggregation of analysed data that the correlation between " knee height " and " pubic arch minus knee height " or length of thigh is only 24 per cent.* Knee height includes height of ankle, which is considered an independent variable. The correlation between supra-pubic and sub-pubic portions of stature is found to be 30 per cent., and striking differences in the relative lengths of these portions of the body occur in different races of man. Thus Eskimo, Mongoloids, and some American Indian tribes have a relatively long trunk and short legs, while the Australian aborigines and some negro groups have a short

* The calculation of the length of different segments of the body by this indirect method introduces sources of error, as Castle points out, which weaken somewhat Davenport's conclusions regarding the inheritance of stature.

trunk and long legs. Of the supra-pubic region, the supra-sternal or head and neck, and sub-sternal or trunk portion, are independent variables as regards length, with a correlation between them of only 9 per cent. A defect in these data is, however, the use of " sitting-height " as a measurement, and the deduction of certain elements of the stature from that.

Among Davenport's conclusions may be mentioned (1) that matings between people of similar stature yield a less variable progeny than those between parents of unlike stature. This indicates that both tall and short persons carry a number of different factors for stature. (2) The progeny of two short parents are more variable than those of two talls. Hence short persons carry more different factors for stature than talls. This is confirmed by (3) the fact that regression of the filial stature towards mediocrity does not occur when the parents are of great stature, but is markedly present when the parents are short. It is therefore concluded that shortness is due to the presence of certain positive factors which inhibit the growth of various parts, the factors for tallness being chiefly recessive. The time of onset of puberty is also probably an element in determining the stature ultimately reached by the individual.

Lus (1924) has also concluded from a study of 911 scientific couples and their 1,418 children that stature is controlled by multiple factors. He finds that "constitution," stout, normal, or thin, is probably inherited independently of stature.

Certain biometric studies of Harris (1924) on the relation between stature and the length of the appendages have some bearing on the question of independent size factors for different parts of the body. He points out that it is better to measure stature and leg-length, subtracting them to obtain sitting-height or trunk plus head, than to measure sitting-height and deduce leg-length. From measurements of children as well as adults, Harris found the correlation between stature and length of appendages fairly high. Such correlation with leg-length would be expected, since this makes up a portion of the total stature. It is found that in tall individuals the leg-length forms a relatively larger proportion of stature than in short, this being true both for adults and children. The correlation between arm-length and stature is relatively small, prevailingly negative, and sometimes non-significant.

While inherited general growth factors, such as differences in the amount of secretion of various glands, are concerned in determining the adult stature as a whole, other factors are

believed to control independently the length of the various segments which go to make up stature. Hence, according to this view, an individual may be tall because of the presence of general growth factors, or because he happens to have inherited length in each segment of his stature. If this is true, then, of the four segments that combine to form the total stature, any individual may be long in some and short in others. It is commonly stated that certain families have predominantly long trunks and short legs, while others may have short, stocky trunks combined with long or short legs. A child may happen to inherit all the relatively long or short segment-lengths of its two parents, and may thus be considerably taller or shorter than either parent. Thus uniformity is not to be expected in marriages between tall and short people. I know personally of two cases of marriages between a very exceptionally tall man and an exceptionally short woman. In one case the son is tall, though not so tall as his father. In the other the son is exceptionally short, like his mother.

Castle (1922) has criticised these conclusions of Davenport. He made a study of size inheritance in crosses between large and small varieties of rabbits and found the F_1 generations intermediate between the parental races, but nearer the size of the larger parent owing to heterosis or hybrid vigour. The latter phenomenon is well known. It is largely confined to the F_1 of both plant and animal hybrids, and probably occurs also in some first generation crosses of man.* Castle found that in crosses between two small varieties of rabbits, such as Polish and Himalayan, the F_1 was larger than either parent owing to this " hybrid vigour," but the effect was lost in the F_2, which was strictly intermediate in average size. In crosses of either of these races with the much larger Flemish rabbit, the average size of the F_2 was strictly intermediate, but the range of variation was much greater than in F_1. By the application of statistical methods it was estimated that eight or ten independent factors or linkage-systems affected the size.

Extensive measurements were made of weight, ear-length, and the dimensions of several bones. A study of the correlation between these measurements was made, in order to determine whether independent factors govern the size in different parts of the body. The correlation-coefficients obtained were uniformly high, and Castle reaches the conclusion that " the genetic agencies affecting size in rabbits are general in their

* For a discussion of heterosis in hybrids see East and Jones (1919).

action, influencing in the same general direction all parts of the body."

This important contribution of Castle to the subject of size inheritance seems to indicate that, in so far as rabbits are concerned, there is no certain evidence of factors independently influencing the size of particular organs. Castle applies the same views to mammals and man, but not to plants where "hormone action is less in evidence." He regards the view of the genetic independence in size of the various parts of the body as a "sporadic relapse into preformationism," and denies that any lack of co-ordination of organs, such as Davenport has suggested, can arise through the crossing of different races of man. He points out also that the measurements used by Davenport were not sufficiently precise to give reliable correlation-coefficients, and criticises the photographs of a Dinka negro and a Chiriguan Indian as evidence that length of legs and trunk is independently inherited. Castle suggests that there is the same difference in proportions between a boy and a man as between the Chiriguan Indian and the Dinka negro, and that the latter, therefore, merely represents a later stage of development. He believes that Southern Italians are short of stature and short-limbed because they cease to grow early, while Swedes and Scotch are tall and long-limbed because they mature later, in the same way that Flemish rabbits are large and have long ears because of their late maturity. Davenport also recognises general growth factors, and it is evident that the last word has not yet been said on this important subject. What is required is a mass of more accurate measurements.

Two earlier studies by Punnett and Bailey (1914, 1918) on the inheritance of weight in poultry and in rabbits also bear directly on this question. They crossed Gold-pencilled Hamburgs with Silver Seabright Bantams. The F_1 was not quite so large as the larger parent, while in F_2 and F_3 the range of variation is beyond that of either parent—*i.e.*, both larger and smaller birds were obtained. The results were explained on the assumption that four factors affecting weight were present, two of them being assumed to give an increase of 38 per cent. in a single dose, or 61 per cent. when present in the homozygous condition. The other two factors were assumed to give 25 per cent. increase in weight in the simplex condition, and 30 per cent. in the duplex condition. The results are believed to give a clear indication that weight in poultry may depend on the presence of definite segregating genetic factors, and it

is suggested that the increased size of some hybrids is not due to hybrid vigour, but to the bringing together of independent growth factors.

In their later study of weight in rabbits, Punnett and Bailey (1918) made crosses between the large Flemish rabbit and a mixed strain of Himalayan-Dutch-Havana of nearly uniform size. They also made certain crosses between Flemish and Polish rabbits. After making a careful study of the curves of growth in these rabbits, they conclude that " though animals belonging to large breeds may mature more slowly than those belonging to small breeds, it does not follow that age of maturity is closely correlated with size." The very small Polish rabbit is believed to mature a good deal more slowly than a larger form such as the Dutch, and the conclusion is reached that size and early maturity are to some extent transmitted independently. These conclusions are contrary to the view of Castle, who finds, from a study of growth-curves in pure and hybrid races, that in Polish rabbits " the initial weight is less, the growth-rate less, and the completion of growth comes earlier," all these features combining to produce a smaller rabbit.

Pease (1928) has recently completed a more extensive study of inheritance of weight in rabbits. In their crosses of Flemish and Polish rabbits, Punnett and Bailey failed to get the heavier classes of animals in an F_2 numbering 65 rabbits. Castle's results were similar. Pease, after studying the variability of his pure stocks, crossed a Polish doe with a Flemish buck and grew an F_2 numbering 309 animals. The whole range of weights was obtained, from the mean size of the (small) Polish stock to considerably beyond the mean of the (large) Flemish stock. It appears, therefore, that the multiple factor hypothesis is applicable to the inheritance of weight in mammals. From the F_2 population strains were selected, one of which matures in about 172 days and the other in about 300 days. These two families appear to breed true to this difference. While there is considerable correlation between heavy weight and slow maturing, yet many rabbits have been bred in which no such association existed.

Even if multiple general size factors control the weight in rabbits, yet more evidence is required regarding the nature of the factors which control the length of different segments of human stature, and in how far they may be regarded as independent of each other. There is much evidence in man (see p. 304) that the activities of various endocrine or ductless

glands, such as the thyroid and pituitary, control the size and development.

Castle's data provide strong evidence that in the strains of rabbits he studied general growth factors preponderated over any factors affecting only the size of certain parts. Nevertheless, the effects of a genetic factor are frequently confined almost entirely to one organ, and we see no reason why this should not apply to size factors as well as others. Wright (1918), in a statistical analysis of earlier measurements by Castle of a stock of rabbits which gave strikingly high correlations between skull and leg measurements, brings out correlations which "suggest the existence of growth factors which affect the size of the skull independently of the body, others which affect similarly the length of homologous long bones apart from all else, and others which affect similarly bones of the same limb." The five measurements considered were length and breadth of skull, length of humerus, femur, and tibia. Analysis of the relations shows that in a population of rabbits most of the differences between individuals are those which involve the size of the body as a whole. But there is a certain amount of variation of each bone length independently of all others measured. There are also groups of bones, which vary together independently of the rest of the skeleton. Two such groups are skull length and breadth and the three leg bones. Again, femur and tibia form a group subject to common influences which do not affect the humerus (foreleg). How far these variations were controlled by genetic factors is of course unknown.

In the *Carnegie Institution Year Book*, No. 27 (p. 321), Castle reports further results on the inheritance of size in rabbits. From a preliminary study of the backcross he raises the question whether ordinary genes are involved in size inheritance which shows blending. Nevertheless he agrees that size is inherited through the sperm as effectively as through the egg of the rabbit, hence probably involving the chromosome mechanism.

From an analysis of Castle's extensive data on the growth rates in rabbits, Robb (1929) finds that the specific or percentage growth rate is the same for Flemish, hybrid and Polish males from birth to puberty, but Polish rabbits are only half the size at birth. They are smaller because of one factor effective during gestation, and another which begins during the fourth month after birth. The hybrid adults are inter-

mediate in size, but their growth curve resembles that of the Flemish Giants in its early stages, and that of the Polish in its early retardation. This is interpreted to mean Mendelian segregration between different factors regulating growth processes.

As regards the stage in development when differences in size appear, Painter found no difference in the size of the egg cells of large as compared with small rabbits, but found a difference established in nine-day embryos. Castle has traced this back to the sixth or seventh day, before the primitive streak is fully established and long before any definitive organs are laid down. The difference is said to be recognisable in the size of the blastodermic vesicle and of the embryonic area on its wall before attachment to the placenta. Hence it is concluded that the rate of *differentiation* is no more rapid in large than in small rabbits, but the *growth* of the former is more rapid from the beginning, greater adult size being attained through accelerated growth and retarded puberty. Since this acceleration begins long before endocrine organs appear, it is concluded that endocrine secretions cannot be concerned in the genetics of size inheritance. As regards plants it has been shown (Gates, 1917) that when a large-flowered species is crossed with a small-flowered one, an intermediate F_1 may be followed by later generations in which widely different sizes of flower occur simultaneously on the same plant, and even different lengths of petal in the same flower. This striking result, which has been studied on a large scale in *Œnothera* crosses, shows that in plants, at any rate, organs of widely different size may occur on the same individual as the result of inherited differences.

Another important fact which bears on the whole theory of multiple factors in the interpretation of size inheritance has been brought out by Sumner and Huestis (1921). From extensive measurements of the right and left mandibles, femurs, and pelvic bones of the Californian deer mouse, *Peromyscus maniculatus*, they have constructed curves for the sinistrodextral ratio for each bone—*i.e.*, the relative lengths of the corresponding right and left bones. The range of variation on either side of equality in this ratio is, of course, small in every case, but they are able to show statistically that the difference—*i.e.*, excess of length or weight on the right or left side—is, as might be expected, not inherited from one generation to the next. Nevertheless, if pure races are compared with hybrids, the F_2 generation shows a considerable increase in the variability of these ratios. The authors point out that

this increased variability of the F_2 in characters which are demonstrably non-hereditary weakens the force of the evidence usually offered in favour of the hypothesis of multiple factors in size inheritance.

Fantham (1924) has compiled an interesting pedigree (Fig. 9) of a tall family in South Africa. All members, both men and women, would be regarded as tall, some of them

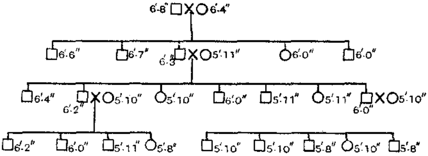


FIG. 9.—PEDIGREE OF A TALL FAMILY. (After Fantham.)

remarkably so, except three in the last generation. Here we have not only inheritance of tall stature but selection of tall mates as well.

The next pedigree (Fig. 10), also from the same source, shows an exceptionally short family in four generations. None of them exceed 5 feet 4 inches, and two of them are under 5 feet in height. Here again there has been mate selection.

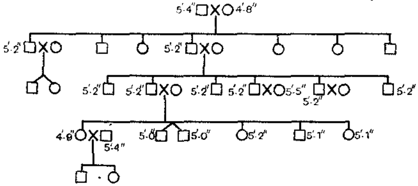


FIG. 10.—PEDIGREE OF A SHORT FAMILY. (After Fantham.)

This family was well nurtured, of good social position, and without cousin marriages. The six sons in the third generation were all about 5 feet 2 inches high, and this was regarded as the "family size." The members of this parentela were also small as children, since at school they were nicknamed the "pygmies." If the factors for shortness in this family are

dominant, it is unlikely that the original parents and the short mates afterwards selected from other families were all free from recessive factors for tallness. It is much more probable that in this family a strong dominant factor for short stature is present.

That the stature of races may undergo changes through selection or improvement in environment has often been stated, but there is very little definite evidence to prove it. Thus it is said that the mean stature in France was reduced several inches by the Revolution and the Napoleonic wars. Improvement in the quality or abundance of food or in other conditions has been supposed to lead, on the other hand, to increase of stature.

LeBlanc (1928) has studied the statistics concerning height in Japanese, taken from the annual statistics of all youths in Japan who have reached the age of twenty years and are measured for military service. His results are based on measurements of about half a million males of twenty each year from 1892 to 1926 inclusive. He finds that the mean height has increased during this period by 3·23 cm.—*i.e.*, from 156·29 cm. to 159·52—the increase being steady and nearly uniform from year to year. The average weight tends also to increase slightly, but not so fast as the height, and the tallest Japanese youths appear to be slightly lighter in weight now than in 1927. The cause of increased height is to be attributed possibly to a greater use of tables and chairs instead of sitting on their own legs; or it may be the result of changes in diet. More dairy products and meat, and a wide range of fruit and vegetables, have been eaten in the last fifteen years. Thus even where a slow increment in stature is indicated it is not easy to determine the causes.

As regards human dwarfs, they may be achondroplasic*—having short legs and long trunk—or ateleiotic,† with normal proportions and reduced size (miniatures). The former condition frequently skips a generation, and its heredity is uncertain, but it appears to be connected with derangements of the internal secretions. A number of pedigrees of both types of dwarfs are described in the *Treasury of Natural Inheritance* (Pearson).

Bangson (1926) gives a pedigree (Fig. 11) of achondroplasia

* Achondroplasia is a defect in the formation of cartilage at the epiphyses on the ends of the long bones, producing dwarfs.

† Ateleiosis is arrest of development before it is complete.

in five generations, descended from three brothers who emigrated from Scotland to Virginia, one of whom was a dwarf. The condition is evidently inherited, but irregularly. In the last generation it behaved as a dominant, but it skipped the third generation—*i.e.*, was inherited as a recessive in III. 5, as also in II. 2, who had only normal children. Again, in I. 2 it was transmitted as a recessive. Possibly something else in the inheritance determines whether or not it shall appear in a heterozygous individual.

Myths of dwarf races are of ancient origin in Scotland, Ireland, Germany, and Scandinavia (Niebelungen). The frescoes of Pompeii and the sculptures of Egyptian tombs show the occurrence of dwarfs. Pygmy human skeletons are found among neolithic burials in Switzerland and France (Poucet and Leriche, 1903). The evidence of the Central African and other pygmy races shows that the condition is an early one in mankind.

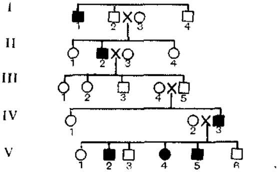


FIG. 11.—INHERITANCE OF ACHONDROPLASIA. (After Bangson.)

Rischbieth and Barrington (1912) have accumulated an enormous amount of information regarding dwarfism in the human race, with a number of pedigrees of its inheritance. Regarding achondroplasia, the condition may appear "accidentally," or it may be hereditary. Cases are known in which normal and achondroplasic babies occur in the same twin birth. The condition appears more commonly in girls than in boys, Kassowitz finding twenty-five girls and four boys in a total of twenty-nine cases. An achondroplasic mother may have children like herself or normal, and delivery must be by Cæsarean section.

Ateleiosis or true dwarfism is considered to be rather rare. It is probably due to a defect of the pituitary. "There is a fair number of cases recorded in which offspring have been born to parents one or both of whom were ateleiotic. These,

however, with the exception of the cases quoted, have grown to a normal size, if they survived to adult years." Usually the condition is found in only one generation. In an exceptional case, an achondroplasic mother produced an ateleiotic son by an ateleiotic father. In another case, ateleiosis occurred in father and son, and probably in the grandfather.

A condition in plants, which appears to correspond with achondroplasy, has been described in cotton, under the name brachysm (Cook, 1915). It consists in a great shortening of the internodes without any corresponding reduction in the diameter or in the size or number of other organs. This condition exists in the " bush " varieties of various vegetables and cereals such as beans and peas, tomatoes, oats, and wheat. Kempton (1921) has studied it in maize, and finds that it is inherited as a simple recessive in crosses with the normal tall.

Ateleiosis* in man appears to correspond to many of the ordinary dwarf varieties of plants and animals, though Davenport thinks it is due to dominant inhibiting factors. In some plants at least smaller cell size is involved. A well-known pedigree of the ateleiotic type of dwarfism occurs in two families in the Tyrol which have intermarried, and Pearson suggests that it may here be inherited as a recessive from an ancestral stock.

Dwarfing of the type which produces general reduction in size is often the result of unfavourable conditions or general inhibition to growth. The Japanese method of producing dwarf trees by starvation is sometimes followed by nature. When a tree seedling germinates in a cleft of a rock where little nourishment is obtainable it may struggle on for decades, making an infinitesimal amount of growth each year. Various instances are known in which domesticated animals in becoming feral under a rigorous climate have decreased conspicuously in size. This is probably the history of the Shetland ponies as well as the English ponies of Dartmoor. Numerous islands have their special breeds; thus Sardinia, Corsica, and many of the larger islands of the Indian Archipelago; while Borneo and Sumatra are said to have several. The history of the ponies from Sable Island, Nova Scotia, can be traced. These are known to be descended (St. John, 1921) from horses taken to this desolate little island from Massachusetts. The history

* Among horses, most ponies, such as the Shetland variety, appear to be ateleiotic miniatures, while the Chinese pony, with short legs and stout body, is apparently an achondroplasic dwarf.

of these horses and other feral animals on Sable Island is of such interest, in showing how a group of animals may react when removed from the care and selection of civilised man, that I refer to the subject at some length. The facts are taken from St. John (1921) and Gilpin (1864).

Sable Island is a long crescent of sand dunes, now twenty miles long and less than a mile wide, about 150 miles east of Halifax, Nova Scotia. When first visited in the sixteenth century, it was apparently ten miles longer and two miles wide. Every few years a great storm washes away some part of the island. The higher dunes now reach nearly 100 feet, but were formerly higher. It is surrounded by shoals, and hundreds of wrecks have occurred on its shores, giving it the lugubrious distinction of being the "graveyard of the Atlantic." On this inhospitable island the Portuguese landed cattle and pigs about 1520. In 1633 a writer reported "about 800 cattle, small and great, all red, and the largest he ever saw."* Large numbers of wild cattle were afterwards shipped from the island, according to a letter written in 1686, and in 1738 there were no cattle left there. Evidently the cattle never became so truly feral as the horses, which were landed afterwards. Unlike the latter, they sought shelter from human habitations in storms, also they *increased* in size and remained uniform in colour. The hogs also ran wild, and became quite fierce. But they were all destroyed in 1814, "because of their ghoulish tastes when shipwrecks occurred." English rabbits, as well as rats, cats, dogs, and foxes, were introduced in turn, the native red and black foxes having become extinct. These introductions furnish an instructive instance of how one species may prey upon and quickly exterminate another.

But the history of the horses is of greatest interest. In 1753 there were twenty or thirty horses on the island descended from animals landed some time earlier. About 1760 Thomas Hancock, a Boston (Mass.) merchant, landed horses, cows, sheep, goats, and pigs. By the end of the American Revolution, all had been killed except a number of horses. Many of the horses, as well as other animals, had been eaten as food by shipwrecked mariners. The horses descended from this stock are well described by Gilpin (1864), who visited the island about 1864, and found some 400 wild ponies in about six herds, each headed by an old male with masses of mane and tail. Each

* Similarly the feral cattle on the Falkland Islands at the time of Darwin's visit in the *Beagle* were of exceptionally large size.

herd had its own feeding ground, and they separated again when driven together promiscuously. The males often fought savagely, and they appeared to sleep standing and never to lie down to rest, always fleeing from man and shelter. Thus in one hundred and fifty years or less they had returned to the habits of the wild tarpany horse, with which they agreed in size, hairy heads, and thick coat, though differing in form in some respects. They are said to reproduce wonderfully the forms of horses known only from the sculptures of Nineveh and the friezes of the Parthenon, having the same short cock-thrappled neck, hairy jowl, and horizontal head. As regards colour, bays and browns were most numerous, then chestnuts, a few blacks, no greys, one probable red roan, one pure white, many piebald, and many " bluish mouse colour,"* often with a black stripe along the back, but none with black lines around the legs.

The striking features in the history of these horses appear to be (1) the complete reversion to an ancestral condition, with change of form and decrease in size; (2) the large number of colour varieties. Mere inbreeding will not account for the former. The colour varieties may, perhaps, all have been represented in the germ plasm, the piebald and bluish colours being extremely old. Piebald horses have existed in all ages. According to Gilpin, they are depicted on the most ancient coins of China and were contemporary with the siege of Troy, being still seen feral in Northern Italy. They have also appeared in Patagonia and among the horses of the North American Indians. The structural changes involved in the reversion of these Sable Island ponies must have resulted in some way from the rigorous conditions. How the environment acts in such cases is not clear. It may be partly by direct inhibition of development, and partly by selection of smaller varieties requiring less food. It may also involve the reappearance as fresh mutations of conditions which had previously been selected out of the germ plasm by the action of man. The small human races in some inhospitable climates may, perhaps, be accounted for in a similar way—*i.e.*, by the selection of variations, sometimes negative, which made survival more likely, as well as by the direct inhibiting effects of unfavourable conditions. But this is obviously not the place to analyse such possibilities from the evolutionary point of view.

* This " Phrygian cerulean blue of Homer " is scarcely known among modern domestic breeds.

That the diminution in size of a species may happen very quickly is shown by garden vegetables which are allowed to run wild, or by the immediate and rapid increase in size of wild species taken into a garden. This appears to be due to the fact that conditions of culture permit of the rapid accumulation of reserve material. Such instances as the following in animals show rapid decrease in size: Dr. John D. Caton (1887) tells how a male and four female wild turkeys were sent from his grounds in Ottawa to Santa Cruz Island, twenty miles off the coast of California. This island is thirty miles long and five to ten miles wide. Here the turkeys had no enemies except a small grey fox. In a few years they became very abundant and very much smaller, the largest weighing not over six pounds, or less than one-third the size of the first and second generations bred there. In this case the mild climatic conditions could not have been responsible, the food supply was abundant, the birds were vigorous and healthy, and there was no evidence of any epidemic. The wild turkey was formerly abundant in Arizona, and birds introduced on the mainland of California north of San Francisco were prolific and of normal size. The cause of the decrease in size of the Santa Cruz birds, therefore, remains unexplained.

An even more striking instance of remarkable multiplication in numbers and decrease in size is described by Huey (1925). Guadeloupe Island, 150 miles off the coast of Lower California, was formerly a naturalist's paradise. By 1830 the fur seals had been nearly exterminated, and in the eighties they became extinct, though the elephant seal escaped complete extinction. The sealers introduced cats and mice, and the whalers who came here later introduced goats. The goats multiplied in vast numbers and devoured every green thing within reach in the primeval forests. They even climbed trees and swam in the ocean for food, and at the last report were destroying the cypresses, which will have the effect of cutting off their necessary supply of water. Early in this century "vast numbers" of goats were killed for their hides and tallow, but without appreciably affecting their abundance. During the war they were again exploited, but "over-population had had its effect upon the size of the goats and the quality of their flesh." It would be interesting to know how diminutive they have become. In 1925 the goat population was estimated at 50,000.

To return to human stature, Davenport concludes that "in both ateleiosis and achondroplasia in man there are

multiple dominant (growth inhibiting) factors, whose actions are often obscured by opposing epigenetic growth factors, and which are probably of a different sort in ateleiosis than in achondroplasia, for achondroplasia affects chiefly or exclusively the appendages." Evidently much has yet to be learned of the inheritance of these conditions in man, as well as concerning the effective environmental factors which are involved in producing racial differences in stature.

A condition which bears some resemblances to achondroplasia, but was probably of a different character, appeared in a flock of sheep in 1791 (Humphreys, 1813). The so-called Ancon sheep originated from a single ram in the flock of a farmer in Massachusetts, near Boston. This ram had short, bandy legs and a short back. The character was evidently a simple Mendelian recessive, and had probably been carried in the stock for some time before it was brought out by inbreeding. The breed seems to have attained some popularity because they could not jump fences; but their crooked forelegs, loose joints, and flabby subscapular muscles made them difficult to drive to market, their carcasses were smaller, and they became extinct some time after 1813. This is an excellent example of man's power over variations in domestic animals, first to multiply them and afterwards to bring about their extinction when they were found less serviceable.

A somewhat different account of the origin of this breed was given by Timothy Dwight (1822, vol. iii., p. 134). He says that about 1798, in Mendon township (Mass.), about eighteen miles south-east of Worcester, "an ewe belonging to one of the farmers had twins, which he observed to differ in their structure from any other sheep in this part of the country." The twins are said to have been of different sex, and to have been bred together to produce the new race. Dwight stated that their bodies were thicker and more clumsy, they were more gentle, and have since multiplied to many thousands; when crossed with other breeds they always resembled entirely either the sire or the dam.

Wriedt (1926) describes what is apparently the same type of lamb as appearing in Eastern Norway in 1919. The parents were mixed Cheviots, and it had very short legs with abnormal knee-joints and could only take a few steps without resting. Another Ancon lamb appeared in Western Norway in 1920. This condition probably represented a single recessive factor. The question arises whether these are independent mutations

or whether the condition has been carried so long in the germ plasm of domestic sheep.

The dachshund among dogs appears to have resulted from a similar mutation, although here the back is long, as also in the turnspit. A variety like the turnspit, having crooked legs and a long back, was formerly known among the pariah dogs of India. Other short-legged types in dogs are the Bassett hounds, Scottish terrier, Sealyham terrier, Skye terrier, and Pekingese. In Bassett hounds and the dachshund short legs are known to be dominant to long, while in the sheep, as we have seen, they appear to be recessive. Horses and Indian zebu cattle with short legs have also been reported.

To quote some of the further conclusions of Davenport regarding heredity of stature in man, he finds that the time of onset of puberty is probably an element in determining the stature ultimately reached by the individual, and that the factors for tallness are mostly recessive—probably due to the absence of inhibitions to prolonged growth. The least variable offspring are, therefore, the children of two tall parents, all being usually tall, while tall mated with short will give the most variable result owing to the recessive factors for greater stature carried by the short parent.

An interesting experimental result bearing on the subject of gigantism has recently been obtained by Uhlenhuth (1921). He fed young salamanders (*Amblystoma*) on a pure diet of the anterior lobe of the hypophysis (pituitary*) of cattle, control animals being fed with earthworms. A greatly increased rate of growth resulted, and when the normal adult size was reached growth continued at a decreasing rate, until animals of gigantic size were produced. The hormone† from the anterior lobe of the hypophysis not only accelerates growth, but also maintains growth after the normal adult size is reached. Carrel finds that in tissue cultures the growth of the cells of warm-blooded animals is not accelerated by hypophysis extract, and various investigators have shown that the division rate of protozoa is not affected by the extract. The continued growth of the salamander is evidently due to continued cell

* The pituitary is a small reddish ellipsoid organ in a depression (the sella turcica) at the base of the skull. It consists of anterior and posterior lobes.

† A hormone is a chemical substance produced as an internal secretion in a gland or organ and carried in the blood-stream in minute quantities to control the activity of another organ.

multiplication rather than increase in the size of cells, the hormone effect being probably not directly on the cells of the body, but through the intermediary of some other substance which stimulates cell growth and division in all the tissues.

Dr. O. Kamm (*Hormones of the Pituitary Gland*, 1929) has recently found that the posterior lobe of the pituitary contains two hormones, which he calls α and β hypophamine. The α hormone aids childbirth, while β raises the blood pressure and controls the output of water by the kidneys. Individuals are therefore to be classified as physiologically wet or dry, the former being extremely sensitive to the β hormone. The fleshy person is almost invariably "wet" and the slender person "dry." Hence fleshiness or leanness may be partly determined by the post-pituitary hormone present. Certain types of fleshiness may, therefore, be likened to succulence in plants.

The data of inheritance of gigantism in man include some interesting cases in the tall Scotch population of North Carolina and Kentucky. It is concluded by Davenport that excessively tall stature is the result of inherited excessive activity in the pituitary gland, the factors for tallness being mostly recessive, due to absence of inhibition to prolonged growth. It is clear that gigantism and dwarfism are not merely the extreme terms in a single series, but they are conditioned in inheritance by entirely different physiological and developmental processes.

Windle (1891) quotes from Francesco Leporatá the case of a dwarf born of normal parents. At the age of 83 years he was 1·130 metres high. By a normal wife he had six children whose heights are given. They were all dwarfs but one normal daughter, their heights ranging around that of the father. One son, Antonio, married twice, both wives being normal. By the first he had a normal daughter, and by the second three children who were below normal. Another son, Pietro, married a normal woman and had three small children, all of whom when measured were below the normal height for their age. Dwarfing in this family appears to be strongly dominant.

Stature is, of course, also a racial characteristic. The tall races are found in North-Western Europe, the Polynesians, North American Indians, and some negro tribes of the Soudan and Central Africa. Their height is 68 inches or over. The short races comprise those of Indo-China, Japan, Malaya, the Hottentots, and Eskimos. Many dwarfs are small because

they cease growth at an early age; others are very small at birth and grow slowly. According to Davenport (1917), the average stature of man ranges from 4 feet 6 inches in the Negrillo Akkas to 5 feet 10 inches in the Scots of Galloway. Frederick Wilhelm of Prussia contemplated breeding a race of tall grenadiers for his battalions, and Catherine de Medici is said to have endeavoured to produce a race of dwarfs by bringing about matings between them.

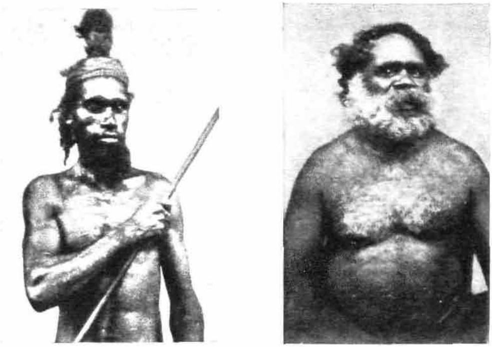
Body Types.

As a subject closely involved with stature and size we may consider certain questions of body type. Various attempts have been made to classify individuals into different types, but it is usually found that these types grade insensibly into each other and not much value can be attached to them. Viola makes a grouping into macrosplanchic (with thick body), microsplanchnic (thin body) and normal, each of the first two making up about a quarter of the Venetian population; but he recognised the existence of intermediates forming a continuous series. Manouvrier divided French people into tall and short or macroskeletal and brachyskeletal types. Beneke similarly writes of phthisical and carcinomatal types. Bean finds two corresponding types, hyperontomorphic and mesontomorphic. A third type—hypontomorphic—does not occur in Europe at all, but in tropical and arctic countries. Sigaud named four types—respiratory, digestive, muscular, and cerebral—recognising in each a particular type of face as well as body form. Kretschmer (1926) has three classes, which he calls leptosomic (or asthenic), athletic, and pycnic. Weidenreich (1927), who reviews this subject, adopts a modification of Kretschmer and, using the terms leptosomic and eurysomic, proceeds to show that these types are found in all races.

Weidenreich's conceptions can be most briefly explained by reference to Figs. 12 to 16, which show the differences between the two types as regards skull and general body features. The leptosomic is "narrower" and the eurysomic "broader" as regards face and body. Weidenreich contends that the two types of face can be combined with every type of skull—*i.e.*, that there is no correlation between the cephalic index and the physiognomy, but the latter is associated with the corresponding type of body build. From numerous photo-

FIG. 12.—EUROPEAN LEPTOSOMIC SKULL TYPE. (From Weidenreich's *Rasse und Körperbau.*)

FIG. 13.—EUROPEAN EURYSOMIC SKULL TYPE. (From Weidenreich's *Rasse und Körperbau.*)



(a) (b)

FIG. 14.—LEPTOSOMIC (a) AND EURYSOMIC (b) TYPES OF AUSTRALIAN NATIVES. (After Weidenreich.)

FIG. 15.—SWEDISH NEOLITHIC MALE SKULL, LEPTOSOMIC TYPE. (From Weidenreich after Retzius.)

graphs he shows these contrasted types among Europeans, Japanese, Chinese, Kalmucks, Veddas, pygmies from the New Hebrides and New Guinea, Malays, Javanese, Indians, Tamils, Australian natives, Papuans, Amerindians and Eskimos, Zulus, etc., but it cannot be said that the distinction is always convincing. Some tribes, such as the Wahima, are of an extremely tall leptosomic type. The same differences are traced in the dynastic Egyptians, as well as the classical Greeks and Romans, and in palæolithic and neolithic skulls. The only doubt is as to whether intermediate and aberrant types may not occur so frequently as to destroy any fundamental value of the distinction. Weidenreich regards the occurrence of

FIG. 16.—SWEDISH NEOLITHIC MALE SKULL, EURYSOMIC TYPE.
(From Weidenreich after Retzius.)

these two types as a sign of racial mixture, but if they occur in practically all races their existence would appear to have some other significance.

Stockard (1923) has expressed interesting views with regard to human and animal types and growth reactions. He suggests that the African pygmies, in their childish development, low intelligence, and features resemble cretins lacking in thyroid. In achondroplasic dwarfs thyroid deficiency is regarded as a secondary cause. Rischbieth and Barrington (1912) showed that the condition is already present in the early fœtus, and that it can be inherited through the father.

Such dwarfs frequently die at birth from no known cause, and Stockard suggests that they may be non-viable in the homozygous condition. Achondroplasic dwarfism is a dominant mutation, probably due to an inherited modification of the hypophysis (which regulates growth).

Ateleiotic dwarfs or midgets are infantile, like children of seven, but bright and intelligent. They stop growing when quite young and are also often achondroplasic. Among domestic animals, the King Charles spaniel and some other tiny breeds of dogs are of this type, as is also the bantam fowl.

Giants may also be well-proportioned but of super-normal growth, as the Great Dane among dogs. But just as midgets often show achondroplasia, so giants usually show acromegaly. Achondroplasia and acromegaly are regarded as opposite extremes in bony growth associated with definite states of the hypophysis, the normal condition standing between. The St. Bernard and mastiff show signs of acromegaly combined with gigantism, while the bloodhound has acromegaly without gigantism. They therefore represent inherited differences in the gland-functioning.

In development, Stockard recognises a tendency first to attain length and then breadth. He classifies ordinary persons as falling into the linear or the lateral type. The linear type is characterised by dolichocephaly, short interpupillary distance, narrow nose bridge, small lower jaw, crowded teeth, long neck, short and narrow trunk, constricted waist, long extremities, active, energetic, nervous type. The lateral type is the antithesis, brachycephalic, eyes wide apart, nose bridge wide, lower jaw-bone large, neck short and thick, extremities not long but with large bones, trunk inclined to be long and full, bulging at the waist. These types have long been recognised. They correspond with Weidenreich's leptosomic and eurysomic types and also with Bean's (1925) hyperontomorph and mesontomorph types.

Davenport (1923) finds a genetical difference between families in the economy of fattening. Some individuals fatten readily, others with difficulty. There must be a difference in their metabolic processes. Obesity often runs in families, and members of one family often undergo similar changes in build through middle life. Relative chest girth was used as a measure of fatness. Two maxima of build were found, one slightly below and one slightly above the average. There are always

a number of short fat people and a number of tall people who have put on flesh; and there is greater variability between the offspring of fleshy parents than of slender parents. It is believed that two pairs of factors are involved in body build, those for fleshy build being slightly dominant over those for slender build.

Similarly in mice, Danforth (1927), finds that the gene for yellow coat colour (which is lethal in the homozygous condition) also causes a pronounced form of adiposity which is more marked in the females. Mice whose ovaries have been removed also develop excess fat.

LITERATURE

Bangson, J. S. 1926. Several generations of achondroplasia. *Journ. Heredity*, xvii. 393-395, figs. 3.

Bean, R. B. 1925. Types of man in the yellow-brown race. *Amer. Journ. Anat.*, xxxv. 63-80.

Castle, W. E. 1922. Genetic studies of rabbits and rats. *Carnegie Inst. Publ.*, No. 320, pp. 55, pl. 1.

Caton, J. D. 1887. The origin of a small race of turkeys. *Amer. Nat.* xxi. 350-354.

Cook, O. F. 1915. Brachysm, a hereditary deformity in cotton and other plants. *Journ. Agric. Research*, iii. 387-400, pls. 10.

Danforth, C. H. 1927. Hereditary adiposity in mice. *Journ. Hered.* xviii. 153-162, figs. 8.

Davenport, C. B. 1917. Inheritance of stature. *Genetics*, ii. 313-398 figs. 19.

Davenport, C. B. 1923. Body build and its inheritance. *Proc. Nat. Acad. Sci.*, ix. 226-230, figs. 5.

East, E. M., and Jones, D. F. 1919. Inbreeding and outbreeding: their genetical and sociological significance. London and Philadelphia: Lippincott, pp. 285, figs. 46.

Fantham, H. B. 1924. Heredity in man: its importance both biologically and educationally. *S. African Journ. Sci.*, xxi. 498-527, figs. 15.

Gates, R. R. 1914. Galton and discontinuity in variation. *Amer. Nat.*, xlviii. 697-699.

Gates, R. R. 1917. Vegetative segregation in a hybrid race. *Journ. Genetics*, vi. 237-253, pl. 1.

Gilpin, J. Bernard. 1864. An introduced species of Nova Scotia. *Trans. N. S. Inst. Sci.*, i. 60-68.

Harris, J. Arthur. 1924. On the relationship between stature and the length of the appendages in man. *Amer. Nat.*, lviii. 254-271, figs. 4.

Huey, L. M. 1925. Guadeloupe Island: an object lesson in man-caused devastation. *Science*, lxi. 405-407.

Humphreys, Col. David. 1813. On a new variety in the breeds of sheep. *Phil. Trans.*, 1813. 88-95.

Kempton, J. H. 1921. A brachytic variation in maize. *U.S. Dept. Agric.*, Bull. No. 925, pp. 28, pls. 19, figs. 8.

KRETSCHMER, E. 1926. Körperbau und Charakter. Berlin: Springer.

LE BLANC, T. J. 1928. The heights of youths in Japan. *Sci. Rep. Tohoku Imp. Univ., Biol.*, iii. 679-687.

LUS, J. 1924. On the question concerning inheritance of stature and constitution. (Russian, with English summary). *Bull. Bur. Eugen. Leningrad*, ii. 49-59.

PEASE, M. S. 1928. Experiments on the inheritance of weight in rabbits. *Journ. Genetics*, xx. 261-309, figs. 24.

POUCET, A., and LERICHE, R. 1903. Nains d'aujourd'hui et nains d'autrefois. Nanisme ancestral. Achondroplasie ethnique. *Bull. de l'acad. de Med. Paris L.* 3rd series, xlix. 174-188, figs. 2.

PUNNETT, R. C., and BAILEY, P. G. 1914. On inheritance of weight in Poultry. *Journ. Genetics*, iv. 23-39, pl. 1, figs. 3.

PUNNETT, R. C., and BAILEY, P. G. 1918. Genetic studies in rabbits. I. On the inheritance of weight. *Journ. Genetics*, viii. 1-25, figs. 12.

RISCHBIETH, H., and BARRINGTON, AMY. 1912. Dwarfism. "Treas. Human Inheritance" Pt. vii. 355-573, pls. 35.

ROBB, R. C. 1929. On the nature of hereditary size limitation. I. Body growth in giant and pigmy rabbits. *Brit. Journ. Exp. Biol.*, vi. 293-310, figs. 6.

ST. JOHN, HAROLD. 1921. Sable Island, with a catalogue of its vascular plants. *Proc. Boston. Nat. Hist. Soc.*, xxxvi. 1-103, pls. 2.

SCHMIDT, ALEXANDER. 1892. Zur Kenntnis des Zwergwuches. *Arch. f. Anthrop.*, xx. 43-81, figs. 11.

STOCKARD, C. R. 1923. Human types and growth reactions. *Amer. Journ. Anat.*, xxxi. 261-288, figs. 3.

SUMNER, F. B., and HUESTIS, R. R. 1921. Bilateral asymmetry in its relation to certain problems of genetics. *Genetics*, vi. 445-485, figs. 5.

UHLENHUTH, E. 1921. Experimental production of gigantism by feeding the anterior lobe of hypophysis. *Journ. Genl. Physiol.*, iii. 347-365.

WEIDENREICH, F. 1927. Rasse und Körperbau. Berlin: Springer, p. 187, figs. 201.

WINDLE, B. C. A. 1891. Teratological evidence as to the heredity of acquired conditions. *Journ. Linn. Soc., Zool.*, xxiii. 448-502.

WRIEDT, CHR. 1926. Das Anconschaf. *Zeits. f. ind. Abst. u. Vererb.*, xxxix. 281-286, figs. 6.

WRIGHT, SEWALL. 1918. On the nature of size factors. *Genetics*, iii. 367-374.

CHAPTER IV

INHERITANCE OF EYE COLOUR AND HAIR COLOUR

As regards eye characters, it may be said that a remarkably large range of abnormalities of the eye are now known to be inherited in the most accurate detail as simple Mendelian dominant, recessive, or variously sex-linked characters. Eye colour was the first human character in which Mendelian inheritance was suggested independently by Davenport (1907) and Hurst (1908). Hurst examined with a hand lens the eye colour of the population of an English village and classified eyes as duplex or simplex according to the presence or absence of brown pigment on the anterior surface of the iris.

With further observations the subject of eye colour in man was seen to be greatly complicated, and we will shortly deal with some of the later developments. Davenport (1927) states that he finds difficulty in applying Hurst's classification in certain cases and doubts if it can always be done.

De Candolle (1884) appears to have been the first to study eye colour. He examined brown and blue eyes in Germany, Belgium, and Switzerland. He found that families from brown × brown gave 80 per cent. of children with brown and 20 per cent. with "clear" eyes. Similarly blue × blue gave 4 per cent. to 12 per cent. of dark eyes, brown × blue gave brown and blue in equal numbers, a brown-eyed mother having more brown-eyed children. He thought that grey was a mixture of brown with blue. It may be pointed out that Pearson and Lee (1900), in a biometrical study of eye colour, drew various conclusions and were the first to point out that the mean eye colour of man is lighter than that of woman. Galton, still earlier (1889), used eight terms for classifying eye colour.

Eye Colour.

The Mendelian studies of eye colour up to 1912 were summarised by Hurst (1912). He defined three patterns of

distribution in the pigmented eye: self-coloured, where the brown is distributed all the way to the periphery of the iris; ringed duplex, in which the brown is confined to a ring around the iris; and spotted duplex, in which irregular spots and patches occur on a blue background. The blue or grey colour represents absence of brown pigment, and is simply the apparent colour of the muscle fibres in the iris as seen through the cornea.

Davenport (1927), in a recent review of eye colour inheritance, states that the stroma or outer layer (connective tissue) of the iris is of mesenchymatous origin and is in front of the ectodermal part of the iris. In complete albinos it is devoid of pigment and hence red from the blood vessels. Pigment in the retinal or inner layer of the iris gives a blue colour to the iris, which depends upon the reflection from particles of the iris and is heightened by the presence of a blue reflecting surface, as when a lady wears a blue dress her eyes are deeper blue. Davenport states that the yellow eye of cats is due to a golden yellow iris pigment. He finds a similar pigment in man, often in blotches on a blue background, uniform distribution giving a green eye. Davenport thinks this yellow pigment is different from the brown melanin and the same as in a yellow (Mongol) skin. He suggests that it may be caused by a basic enzyme (I), tyrosinase, acting alone on a chromogen (amino acid), brown being due to the action of two enzymes (I and II) on the chromogen. Both the chromogen and the enzyme would be produced by catalysators located in certain genes, these catalysing enzymes being the inheritance elements, they in turn producing the chemical groups which react to form the pigment. The yellow has usually been regarded simply as a dilution of the brown. Galloway (1912), for instance, held this view. Davenport gives various details of observation with a hand lens, which show a continuous phenotypic series from blue eyes to black, and concludes that many genotypic factors are probably concerned in eye colour. It can hardly be otherwise when we consider the large number of eye colour mutations in Drosophila, forming a close series genetically independent.

Iljin (1926) describes a new eye colour—ruby—in man. This type of eye is now known in the guinea-pig, mouse, rat, cat, dog, and man. Iljin observed it six times in man and found that it could occur with either fair or dark complexion.

The eye colour undergoes slow changes throughout life In European babies the eyes are blue and may gradually become

darker during childhood, reaching their definitive colour at about eight years of age. The state of health also affects the pigmentation. The evidence of Winge (1921) that brown eye colour may be inhibited by eye abnormality is regarded by Davenport as weak. But an injury to the lens or the retina causing blindness may be followed by the entire resorption of pigment. In old persons the eye colour may change from brown to pale bluish by absorption of melanin, as in grey hair. In Indians it has been observed (and I can confirm this) that in old age a blue ring develops around the very dark eye through peripheral absorption of pigment.

The blue eye presumably originated through a mutation from the brown. This may have occurred but once and has been perpetuated in the Nordic, East Baltic, and probably also in certain Northern Asiatic races referred to by Jochelson (1918). E. Fischer suggests that loss of eye pigment is a domestication phenomenon, but there are innumerable other loss mutations in wild races of plants and animals. Davenport concludes that there are two principal classes of eye colour—blue and brown; that blue is recessive to grey and grey to brown.

An earlier paper (Boas, 1919) presents statistics of eye colour which, it is claimed, do not support the Mendelian contention that two blue-eyed individuals have only blue-eyed offspring. But the writer admits that in collecting these data, persons with a certain amount of brown in their eyes may have been classed as blue-eyed. Pearson and others have also studied carefully some of the more detailed differences in eye pigmentation which are important for a complete analysis. It is clear that the early conception of a single Mendelian factor difference between brown and blue eyes is only a rough first approximation in the study of this subject.

Dürken (1925) gives a pedigree of two "clear-eyed" parents with one brown-eyed and one clear-eyed boy. But since he has not examined them himself and uses such a loose term as clear-eyed, no value can be placed on his work. We may conclude that no case of brown eyes from really blue-eyed parents has yet been shown.

Usher (1920), from a careful histological examination of six albino eyeballs, found traces of pigment in four. The fifth was unknown, and the sixth, that of an infant, was devoid of pigment. Usher therefore concludes that total absence of pigment cannot be used as a definition of albinism in man.

The *fovea centralis** in albinotic eyes is shown to be absent or imperfect, and this may be the chief cause of the imperfect vision in such eyes. In the eyes of albinotic individuals belonging to dark races the mesoblastic pigment appears earlier and is found in much larger quantity at time of birth than in European eyes. Chemical examination indicates that there is more pigment in the eyes of albinos of dark races than of white races. This is in line with much evidence from mammals of a close relation between density of coat colour and of eye pigmentation.

Later studies of brown and blue eyes indicate that they are not always a simple pair of Mendelian characters as formerly supposed, but sex-linkage and other complications may come in. Bryn (1920) collected statistics in Norway and states that in four out of thirty marriages two blue-eyed parents had some brown-eyed children. From these four marriages there were ten children with brown eyes and seventeen with blue. One or both grandparents, in all cases, had brown eyes. Winge (1921), in a much more extended study, criticises these results and concludes that such cases are exceedingly rare if the parents have normal vision. By means of a questionnaire, Winge collected data of eye colour in about 1,400 children of natural history association members in Denmark and their parents. The data obtained were carefully sifted, and the results are given in the table on p. 62.

From the table it will be seen that, in addition to the seven children with doubtfully blue eyes from blue-eyed parents, twelve children (belonging to eight families) had brown pigment in their eyes. Further information obtained from five of the families indicates that the condition was due in two cases to abnormalities in the eye. In another family of seven, two of the daughters had some brown pigment in their eyes, and one of the latter married a blue-eyed man and had six children, all blue-eyed. This case is thought to be explained by assuming that one of the grandparents was genotypically† brown-eyed but had a "pigment restrictive disposition" which made him or her phenotypically (that is, visibly) blue-eyed. The brown-eyed daughter having blue-eyed children is explained by sex-linked inheritance. It is shown from other evidence that pigment-inhibiting factors may be accompanied by abnormali-

* This is a pit in the middle of the macula lutea or point of clearest vision at the centre of the retina.

† That is, in inherited germinal constitution.

ties in vision, but the interpretations in this part of the paper are not always convincing.

TABLE II

INHERITANCE OF EYE COLOUR (WINGE).

Marriages.	*Number of Children.*			*Total.*
	Blue.	*Brown.*	*Greyish-Green or Bluish-Green.*	
Blue × blue	625	12	7	644
Blue × brown and conversely	317	322	9	648
Brown × brown ..	25	82	—	107
Total	967	416	16	1,399

Perhaps the most interesting results of Winge concern the sex-linked inheritance of eye colour. The statement that there are more brown-eyed women than men was borne out by statistics of 300,000 school children, collected by S. Hansen. Similar results have been obtained by others. Winge shows the fact of sex-linkage by giving the results of marriages in which the parents had different eye colour. These are appended in the following tables:

TABLE III.

MOTHER BLUE × FATHER BROWN.

Eye Colour of Children.	*Sons.*	*Daughters.*	*Total.*
Blue	63	50	113
Brown	65	81	146
Greyish-green or bluish-green	4	2	6
Total	132	133	265

Clearly from the tables, when the father has brown eyes, half the sons have blue eyes and half brown, but many more daughters have brown than blue eyes, although the total

numbers of the sexes are equal. On the other hand, when the mother has brown eyes there is a marked excess of blue-eyed sons and daughters. After an elaborate analysis these results are explained by assuming that in addition to the simple pair of factors originally recognised, there is another dominant factor for brown eyes which is sex-linked in inheritance. The writer is further obliged to assume that female germ cells (b W) containing the sex-linked factor (W) together with the ordinary determiner for blue, cannot exist. It should not be difficult to obtain extensive data of eye colour to test these hypotheses. All the assumptions made are reasonable enough in the light of present genetic knowledge. It is well known that in rabbits and guinea-pigs factors for coat colour also often affect eye colour.

TABLE IV

MOTHER BROWN × FATHER BLUE.

Eye Colour of Children.	*Sons.*	*Daughters.*	*Total.*
Blue	101	103	204
Brown	97	89	176
Greyish-green or bluish-green	—	3	2
Total	188	195	383

Castle (Carneg. Publ., No. 337, 1926) finds that in the white Viennese rabbit blue eye is recessive, and Davenport concludes that in rabbits the factors for brown, grey, and pink eye form an allelomorphic series, while blue eye is apparently independent—in a different chromosome. Similarly in man, brown, hazel, blue, and pink eyes may be a series of multiple allelomorphs.

The writer in 1922 had the opportunity of examining the eye colour of people in Bergen, Norway. Only about one in fifteen would be roughly classed as brown-eyed, but the blues varied continuously from very light to very dark blue, and so through greenish or yellowish shades (due to a small amount of brown pigment) to pale brown, dark brown being rare. Every grade of colour appeared to be represented, with a great predominance of the paler shades.

During the last few years these intermediate eye colours and their inheritance have been given much more attention.

Frets (1925) confirms others in finding that in Western Europe there are more females than males with non-blue eyes. But he finds that in Scotland and South-Eastern Europe (Russia, Bulgaria, etc.) there is no excess of blue-eyed males. Hence the sex-linked factor for brown eyes, assumed by Winge, may be supposed not to have reached there. Frets finds no exception to the rule that blue × blue gives only blue. But he finds difficulty in classifying eyes with traces of yellow pigment, and states that parents with such eyes may have children with more or with orange pigment in the central part of the iris. Frets classifies iris patterns as (1) ring pattern of brown pigment over the sphincter muscle; (2) ray pattern with certain sectors pigmented; (3) spotting pattern with irregular brown pigment spots. Bond (1912) finds that the ray pattern is especially apt to occur when one parent has brown eyes and the other blue.

Philipchenko and Liepin (1922) have made a study of eye colour and hair colour based on a questionnaire sent to the literati of Leningrad. Among 488 parents and 738 children, 22 per cent. were classified as blue-eyed, 42 per cent. grey-eyed (including green), and 35 per cent. dark-eyed. Grey is distinguished from blue by the presence of a factor B, so that grey eyes might be BB or Bb. Cases were recorded in which blue × grey and grey × grey gave children with brown eyes, but these were based on statements of the parents and not on critical observation by the investigators. A factor C is assumed for "dark" eyes and probably an intensity factor D for black eyes. No evidence of a sex-linked factor was found, such as Winge assumed in Western Europe.

Finally, two recent critical papers on eye colour may claim our attention. Bollag (1927), working with Professor Vogt, has made a study of intermediate eye colours in Switzerland, and Bryn (1926) has analysed in greater detail the inheritance of the various shades between blue and brown in Norway. Professor Vogt finds that the children of parents with intermediate eye colours (Mischfarben) are often darker, but may be lighter than either parent. Bollag classifies various agencies that may change iris colour: (1) A rare form of heterochromy-cyclitis, depigmenting the iris to blue; (2) early trauma, which may change a blue iris to brown; (3) siderosis or deposit of an iron compound from some foreign body or from the blood; (4) heterochromidia due to melanosis or excessive pigment development in one eye (rarest); (5) early paralysis of the

sympathetic, lessening pigment deposition in one eye; (6) smaller differences between the eyes may result from variation.

The mixed eye colours are classified as grey-brownish, grey-yellowish, grey, grey-greenish, yellow-greenish, the density of the pigment deposits accounting for the different shades. Martin Rudolf's standard table of colours was used, giving 16 classes between blue and brown, and 84 parents with their 212 children were examined, only families with 4 or more children being studied. In 11 of these families the children's eye colour was between that of the parents, in 7 families some children were intermediate and some lighter, while in 24 families the children's eyes ranged from lighter and intermediate to darker. Bryn and Winge both found cases of children with darker eyes than the parents, but Winge explained them as pathological.

Professor Vogt believes that these intermediate colours are not heterozygotes, but represent *nova* whose origin is not explained by crossing, and he assumes the presence of multiple factors which are independent or coupled. In twenty-five crosses between intermediate colours or conditions, only 42·5 per cent. of the children are nearly the same as the parents; 32 per cent. have darker brown but intermediate eyes, 59 per cent. are intermediate like the parents, and 9 per cent. are more nearly blue than the parents. It is difficult to say in how far the results may be due to the segregation of subsidiary factors and in how far to non-inherited fluctuations. The chief point emanating from Bollag's study appears to be that the various intermediate eye colours are not heterozygotes of blue and brown, but are due to independent stable factors.

The important paper of Bryn (1926), in which he himself examined some 3,000 individuals in Norway and depicts thirty-six different eye types found there, is a critical advance on previous work. He recognises eye types with the pigment in rings, clouds and radial stripes, or diffuse over the whole iris, and concludes that there must be three kinds of factors for eye-colour pattern: (1) pigment-producing factors; (2) pigment-distributing factors; (3) pigment-concentrating factors. Brown eyes are assumed to have a series of factors, K, K′, K″, K‴, for pigment and a series of distributing factors, the albino eye lacking all such factors. A and B are the pigment-distributing factors, a and b giving pigment-concentration. Bryn finds that when the parents have a ring, radial or cloud pattern, most

of the children will have the same pattern. A is assumed to distribute the pigment over the whole iris, and B to be weaker, leading to a cloudy effect. Blue eyes may then be represented by the formulæ AABBKkk′k′k″k″, AaBbKkk′k′k″k″, AaBBKkk′k′k′k″, or AABbKkk′k′k′k″. Hence two blue-eyed heterozygotic parents may have children with intermediate eyes.

Bryn agrees with earlier writers that no normal eye is devoid of pigment, even blue eyes always having a little yellow-brown pigment. There is therefore a variety of types of mixed eye colours, the differences being both quantitative and qualitative (in manner of concentration). Green eyes usually have a denser stroma and a little hidden brown pigment. When one parent has blue eyes and the other has blue eyes with brown pigment radiating from the pupil, then about 25 per cent. of the children will have blue eyes, the others having more or less pigment, partly in a ring around the pupil and partly in radiating stripes. When one parent has very blue eyes and the other a broad brown ring around the pupil, then about 40 per cent. of the children will have blue eyes, 40 per cent. will be like the brown-eyed parent, and 20 per cent. will have blue eyes with a small yellow ring around the pupil. It is also concluded that grey eyes are inherited differently from blue, the children of grey-eyed parents having a much greater chance of brown pigment in their eyes than the children of blue-eyed parents.

Many of the shades of blue found in Scandinavian eyes are paler than the blue eyes usually found in more southerly populations. In the absence of breeding experiments, the inheritance of these smaller differences in eye colour is a matter of great difficulty, if it ever can be fully analysed. But much progress has been made in the last five years, and there is no reason to doubt that the segregation of factors follows the same laws here as elsewhere. Much, however, remains to be done before such an analysis can reach an agreed basis as to the exact nature of the various factors involved.

Sedgwick (1861) describes an interesting family in County Wexford, Ireland, with tortoiseshell-coloured eyes. The third generation, numbering sixteen sons and five daughters, all had the peculiarity, which they inherited from their mother. The mother had three sisters and a brother with the same colour of eyes, which was in turn inherited from *their* mother. Hence the character was a simple Mendelian dominant (Fig. 17).

The condition known as heterochromidia iridis, in which the two eyes are of different colour, was known to Aristotle, who called it heteroglaucus. The earliest paper I have found in which its inheritance is noted was by Osborne (1849). A man with heterochromidia iridis is said to have had fifteen brothers and five sisters, all with the same abnormality. This was derived from his mother, whose three sisters and one brother were in the same condition and got it from their mother's side. It is doubtful if this pedigree is accurate as stated.

Przibram (1908) found that in Angora cats, an animal having one blue and one yellow eye, when crossed with a cat having blue eyes or yellow eyes gave some offspring with heterochromidia iridis and some with symmetrical eye colour. He concludes that animals with asymmetrical eye colour can be traced back to asymmetrical ancestry, and that either eye colour of an asymmetrical parent can appear in symmetrical form in the offspring.

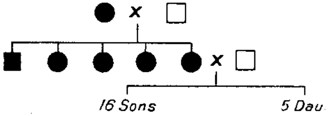


FIG. 17.—TORTOISESHELL-COLOURED EYES.

Gossage (1908) cites a case of human heterochromidia occurring with nine cases in five generations. One eye, always the left, was greyish blue in colour with chestnut-brown patches. As shown by the pedigree (Fig. 18), in four generations there were eight affected and twenty-two free.

Bond (1912) has studied the inheritance of the condition known as heterochromidia iridis, in which the two eyes are of different colour. In addition to the patterns recognised by Hurst, he distinguishes between self colour and the ray pattern, in which only one or more sectors of the iris are pigmented. This condition is a fairly frequent one, and shows inheritance, though the position of the ray or sector is variable from one generation to another. Bond finds that the two eyes are unlike in pigmentation in perhaps one or two individuals per 1,000. In rabbits the condition is much more common, sometimes four in 100. Horses with a " wall " eye are, of course, well known, and in various breeds of dogs, such as Great Danes, English collies,

and Old English sheep dogs, the condition is not uncommon. In both horses and dogs it is frequently associated with a patchy or piebald coat. Both conditions may arise when self colour is mated with white, and in some cases it may be looked upon as a phenomenon of disintegration following on the quantitative dilution of a factor for pigmentation. It resembles in this respect the striping of flowers (see p. 107). Because factors may be diluted and disintegrated in this way by crossing, it is not necessary to assume, as Bond does, that there were originally independent factors for each eye and subordinate factors independently controlling different areas of the iris. There is no evidence that factors have been built up in this way. They appear rather to originate as germinal changes or new conditions of equilibrium, which may later become modified by crossing or otherwise.

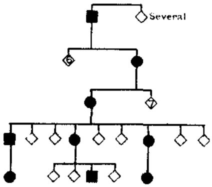


FIG. 18.—INHERITANCE OF HETEROCHROMIDIA IRIDIS. (After Gossage.)

Calhoun (1919) points out that heterochromidia iridis may arise from various causes or (in a small number of cases) may be inherited. He cites a case in which the father and mother are blonde with blue eyes. The baby had a drooping upper right eyelid, that eye being lighter in colour than the other. Seven years later there was some evidence of facial atrophy on the right side, and this iris was blue, while the left one was brown. There seems to be a discrepancy here, as both parents were blue-eyed. He concludes that one-sided paralysis of the cervical sympathetic nerve is inherited and may be a cause of heterochromidia. Punnett (1928) finds that the factor P, producing the higher grades of coat pigmentation in the Dutch rabbit, also inhibits or prevents heterochromidia iridis. Any rabbit without P may show heterochromidia.

A number of observations on the eye colours of birds and

their inheritance are recorded by the same writer (Bond, 1919). His studies were chiefly of pigeons and fowls, although references are made to many other species. The pigment granules producing eye colour may be black, brown, yellow, ruby, or pearl. The " bull " eye owes its black colour, as in the white fantail pigeons, to the absence of pigment from the anterior surface of the iris. The posterior uveal pigment shines through the translucent tissues of the iris and gives the eye its colour, as in blue human eyes. Also, as with blue eyes in man, the " bull " eye of the chick is retained in the adult. The ruddy glow of this eye is due to the plexus of bloodvessels. (A similar type of eye occurs in guinea-pigs of the type which Castle calls red-eyed silver agouti.) But in most birds with dark or black eyes, the colour is due to the presence of anterior iris pigment. In the rock pigeon (*Columba livia*) the iris colour is yellow or orange, while in other pigeons it may be white or red, and in the stock dove (*C. œnas*) the eye is peculiar, its black colour being due to the presence in the iris and in deeper tissues of branching cells packed with dark granules.

In the pearl or white eye of pigeons and the " daw " eye, as in the Malay fowl, there is no anterior pigment in the iris, but its tissues are opaque, owing to the presence of crowded colourless granules. This apparently corresponds with the " wall " eye in horses, dogs, and pigs. The muscle fibres of the avian eye, however, are striated or voluntary, and not plain as in the mammals. Pearl eye in pigeons is recessive to yellow or " gravel " eye, as " daw " eye in fowls is to amber or black eye when the latter is due to anterior pigment. The yellow eye derives its colour from a network of branching cells containing yellow granules. If the latter are closely packed, the eye may appear black. In fowls the yellow eye may be due to (1) granules in the connective-tissue cells; (2) granules in the striated muscle cells, as in Dorkings and Orpingtons. In owls the yellow eye is due to bright yellow granules in cells coating the iris.

Brown and black eyes in birds are produced by a layer of branching cells on the iris containing dark pigment granules. Ruby eyes are produced in various ways in different birds; and some birds, such as certain birds of paradise, have parti-coloured irides. Genetically, black due to pigmented iris is dominant over yellow and other grades of iris pigmentation.

Eye and Hair Colour.

Some advances have been made in the study of the relations between eye colour and hair colour in man. That a correlation exists has long been commonly recognised. Brownlee (1913), by mathematical analysis, concluded that there is linkage between factors for hair colour and eye colour. S. Wright (1918) suggests that, since red hair is associated with light eyes, there are two kinds of dilution in eye colour, one genetic factor reducing the black both in the hair and the iris, and thus allowing red hair to appear, another factor reducing the pigmentation of the iris without affecting the hair, and thus permitting of types with black hair and blue eyes, such as are stated to occur frequently among the Irish. That blue eyes are commonly associated with light brown or flaxen hair is well known. Less frequently "cross-over" types occur, with brown eyes and flaxen hair. In a study of crosses between Indians and whites in Canada (Gates, 1929), it was similarly found necessary to account for mixed-bloods with half skin colour and nearly blue eyes by assuming that certain factors for eye colour were independent of certain factors for skin colour (see p. 343). Haecker (1925) suggested that linkage between hair, eye, and skin colour could be accounted for by linkage and crossing-over of genes lying in the same pair of chromosomes.

Gross (1921) has made a study of the relations between eye and hair colour. He assumes that there is one chromogen (P) for iris pigmentation and another (D) for hair, and an enzyme (F) which activates both. Staffe (1922) has examined the hair and eye colour of 6,072 school children in the Kühlandchen, the original home of Mendel. Philipchenko and Liepin (1923) have made a considerable analysis of conditions as regards hair-colour and its relation to eye colour in Russia. They classify hair colours as blond, chestnut brown, brunette (black), and red, about half the population examined (Leningrad) being brown, one-quarter each blond and black, and 1 per cent. red. They find that blond × blond gives blond, whether any chestnut as well is uncertain. Blond × chestnut brown gives 50 per cent. blond, 50 per cent. brown. Chestnut × chestnut gives about one-quarter blond, many chestnut, and some black or brunette. Blond × black gives two or three

times as many dark-haired (black or chestnut) as blond. They use the following symbols:

Blond hair = bbcc, chestnut = Bbcc, BBcc, bbCc, bbCC.

Black hair = BC, homozygous or heterozygous, usually BbCc.

Red hair = bbcc + a factor hypostatic or recessive to blond (yellow) hair. They assume linkage of a factor for dark eyes and a factor (B or C) for dark hair. They find:

Blue or grey eyes with blond hair in	30·25 per cent.
Blue or grey eyes with chestnut hair in	9·92 ,, ,,
Brown or black eyes with black hair in	42·84 ,,
Blue or grey eyes with red hair in	2·21 ,, ,,

LITERATURE

Boas, Helene M. 1919. Inheritance of eye colour in man. *Journ. Phys. Anthrop.*, ii. 15-20.

Bollag, L. 1927. Untersuchungen über die Vererbung von Mischfarben der Iris beim Menschen. *Arch. Julius Klaus-Stiftung*, ii. 191-205, pl. 1.

Bond, C. J. 1912. On heterochromidia iridis in man and animals from the genetic point of view. *Journ. Genetics*, ii. 99-129, pls. 4, figs. 7.

Bond, C. J. 1919. On certain factors concerned in the production of eye colour in birds. *Journ. Genetics*, ix. 69-81.

Brownlee, J. 1913. On inheritance of hair and eye colour. *Proc. Roy. Soc. Edin.*, xxxii. 458-474.

Bryn, H. 1920. Researches into anthropological heredity. I. On the inheritance of eye colour in man. *Hereditas*, i. 186-212.

Bryn, H. 1926. Ueber die Augentypen in Norwegen und ihre Vererbungsverhältnisse. *Skr. utg. av Det Norske Vidensk.-Akad. i Oslo*, No. 9, pp. 57, pls. 2.

Calhoun, F. P. 1919. Causes of heterochromia iridis with special reference to paralysis of the cervical sympathetic. *Amer. Journ. Ophthalm.*, ii. 255-269, figs. 2.

Davenport, G. C., and C. B. 1907. Heredity of eye colour in man. *Science*, xxvi. 589-592.

Davenport, C. B. 1927. Heredity of human eye colour. *Bibliogr. Genetica*, iii. 443-463.

De Candolle, A. 1884. Hérédité de la couleur des yeux dans l'espèce humaine. *Arch. d. sci. phys. et nat. Genève*, xii. 97-119.

Dürken, Bernhard, 1925. Die Vererbung der Augenfarbe beim Menschen. *Zeits. f. ind. Abst. u. Vererb.*, xxxvii. 67-81.

Frets, G. P. 1925. Over de erfelijkheid van de oogkleur. *Genetica*, vii. 65-86.

Galloway, A. R. 1912. Notes on the pigmentation of the human iris. *Biometrica*, viii. 267-279.

Galton, Francis. 1889. Natural inheritance. London: Macmillan, pp. 259.

Gates, R. R. 1929. A pedigree study of Amerindian crosses in Canada. *Journ. Roy. Anthrop. Inst.*, lviii. 511-532, pls. 5, charts 6.

GOSSAGE, A. M. 1908. The inheritance of certain human abnormalities. *Quart. Journ. Med.*, 1908, i, 331-347.
GROSS, K. 1921. Ueber Vererbung von Augen- und Haarfarbe und den Zusammenhang beider. *Arch. f. Rassen.- u. Gesell. Biol.*, xiii. 164-175.
HAECKER, V. 1925. Pluripotenzerscheinungen. Jena : Fischer, pp. 213, figs. 26.
HURST, C. C. 1908. On the inheritance of eye colour in man. *Proc. Roy. Soc. B.*, lxxx. 85-96.
HURST, C. C. 1912. Mendelian heredity in man. *Eugenics Rev.*, pp. 25, figs. 6.
ILJIN, N. A. 1926. Ruby eye in animals and its heredity (Russian). *Trudy Lab. Exp. Biol. Zooparka, Moscow*, i. 107-129.
JOCHELSON, W. 1928. Peoples of Asiatic Russia. *Amer. Museum Nat. Hist.*, pp. 277, figs. 42, maps 10.
PEARSON, K., and LEE, ALICE, 1900. On the inheritance of eye-colour in man. *Phil. Trans. A*, cxcv. 102-150.
PHILIPCHENKO, J., and LIEPIN, T. 1913. Zur Frage der Vererbung von Augen- und Haarfarbe bei dem Menschen. *Bull. Bur. Eugenics, Petrograd*, i. 10-14.
PRZIBRAM, H. 1908. Vererbungsversuche über asymmetrische Augenfärbung bei Angorakatzen. *Arch. f. Entw.-Mech.*, xxv. 260-265.
PUNNETT, R. C. 1928. Further notes on Dutch and English rabbits. *Journ. Genetics*, xx. 247-260, figs. 6.
SEDGWICK, W. 1861. On sexual limitation in hereditary disease. *Brit. and Foreign Med.-Chirurg. Review*, xxvii. 477-489, xxviii. 198-214.
STAFFE, A. 1922. Untersuchungen über die Augen- und Haarfarbe der Schulkinder des Kühlandschens. *Arch. f. Rassen. u. Gesell. Biol.*, xiv. 305-314.
USHER, C. H. 1920. Histological examination of an adult human albino's eyeball, with a note on mesoblastic pigmentation in fœtal eyes. *Biometrika*, xiii. 46-56, pls. 2.
WINGE, Ö. 1921. On a partial sex-linked inheritance of eye colour in man. *Compt. Rend. Lab. Carlsberg*, xiv. No. 12, pp. 23.
WRIGHT, SEWALL. 1918. Colour inheritance in mammals. XI. Man. *Journ. Heredity*, ix. 227-240.

CHAPTER V

HEREDITARY ABNORMALITIES OF THE EYE

THE literature concerning the inheritance of eye abnormalities has become very extensive. Reference may be made to recent general summaries of this subject by Clausen (1923-24) and Macklin (1927), and to sex-linked abnormalities by Vogt (1922). Much of the most important earlier work was done by Nettleship, who published a summary (1909) of knowledge at that time in a classical paper. He points out that *anticipation* or earlier development of the anomaly in later generations occurred in 14 out of 31 pedigrees. A bibliography of hereditary ocular defects was published by Howe (1921).

Pearson and Barrington (1909) made a biometrical study of the inheritance of vision, as regards the relative influence of heredity and environment. They found no evidence whatever that overcrowded, poverty-stricken homes or ill-conditioned or immoral parents had a markedly detrimental effect on the eyesight of the children. Nor was there any statistieal evidence that the school environment had a deleterious effect on eyesight. On the contrary, they found ample evidence that refraction and keenness of vision are inherited characters.

A condition accidentally discovered in mice and not known to occur in human beings is that in which the retina of both eyes differs from the normal in the complete absence of the outer light-sensitive (rod) layer, great reduction in the number of rows of nuclei in the external nuclear layer, and lesser changes in deeper parts of the retina. Keeler (1927) found this condition in 1923 in a certain strain of albino mice, the rodless retina being shown in one male and eight females of the stock. It first appeared in the offspring of normals, has since bred true for six generations, and behaves as a simple recessive in crosses with normal. It causes complete blindness, but there is no visible lesion of the eye, and the condition can only be discovered from sections. Three conditions of the retina were found, in which the external nuclear layer consisted of 1, 3, or 6 rows of

nuclei, whereas in the normal retina this layer contains 15 rows. The 3-row and 6-row conditions appear to be modifications of the 1-row, perhaps due to a genetic modifying factor.

CONGENITAL STATIONARY NIGHT-BLINDNESS, probably due to a retinal defect, furnishes one of the largest pedigrees known for the inheritance of any human condition. This is the famous pedigree of Jean Nougaret (1637-1719) and his descendants (peasants in the South of France) through ten generations, seven of which were published by Cunier in 1836. Nettleship (1907) worked out the full genealogy to 2,116 persons, recognising the condition as a Mendelian dominant, and the chart of inheritance is given by Bateson (1913) in condensed form. Affected persons are unable to see in a dim light. An affected person always has an affected parent, and both sexes are equally affected. The condition therefore behaves in this pedigree as a simple dominant, but Bateson found that by adding together the offspring from DR × RR matings there is an unexplained excess of normals, in the ratio 130 : 242.

In another family studied by Newman (1913), night-blindness (hemeralopia) is inherited like colour-blindness, as a sex-linked character, being transmitted through unaffected daughters of affected males to some of their sons. This family is from Texas, having originated in North Carolina. In one respect it departs from the typical scheme for sex-linked inheritance, in that there is " apparent non-inheritance of the capacity to transmit night-blindness on the part of the sisters of night-blind men." In F_3 and F_5, if there were no consanguineous marriages, there should be equal numbers of females carrying or not carrying night-blindness. But none of the five married sisters of F_3 night-blind men show any trace of night-blindness in their progeny. Newman suggests that possibly night-blindness cannot be inherited through two successive generations in the female line, owing to prolonged association of the defective X (sex) chromosome with a normal X. The next generation will determine whether this is the true explanation.

In its main essentials the character in this family behaves as a recessive located in the X chromosome, but, as in hæmophilia, there is an excess of abnormals. Thus, of the 36 offspring of the night-blind-carrying daughters of night-blind men, there were 22 ♂, 14 ♀, and of these 22, 17 were affected and only 5 not. In this family the night-blindness is usually accompanied by myopia (short-sightedness), and almost invariably by strabismus (squinting), with frequent occurrence also of

PTERYGIUM.* It is believed that all these conditions form one complex, and whether all appear may depend on other factors present. The pterygium in Newman's pedigree appears to be a simple dominant. Its gene is therefore in an autosome, while that for night-blindness is in the X chromosome.

Nettleship (1912) has also described a family in which night-blindness was sex-linked and was associated with myopia. Another form of night-blindness has been described by Kawakami (1925) in Japan, where it is known as Oguchi's disease. It is found to be inherited as a recessive. It would, therefore, appear that the same condition may arise through an alteration in the sex chromosome or in another chromosome, and may be either dominant or recessive. Night-blindness, or "moon eye," has been described in a herd of shorthorn cattle in Oklahoma (Craft, 1927). They are normal by day, but are so blind at night that they stumble over things. They were descended through inbreeding from a common ancestor, and as normal parents gave some night-blind calves, the condition is apparently recessive.

Day-blindness (nyctalopia) in man is a very rare condition and is always accompanied by colour-blindness and amblyopia (Macklin, 1927, vi.). It is congenital and is supposed to be due to a deficiency of the cones in the retina. In the Nettleship pedigree it is recessive. Sedgwick (1861) cites a case of momentary blindness after bending their heads in a father and two sons. He also refers to the Le Compte family, in which 37 children and grandchildren became blind, like the grandfather, at the age of seventeen or eighteen years.

The pathology of congenital night-blindness is quite unknown, as the eyes function normally by day and never have to be removed. It differs fundamentally from retinitis pigmentosa (*q.v.*) in that it is always congenital and there are no visible changes in the fundus. There is no associated defect except that myopia is frequently associated as a condition inherited in the same males who have night-blindness. Temporary night-blindness, as a non-inherited symptom, may be due to malnutrition, nerve exhaustion, rheumatism, malaria, or other causes. The prescription of liver for night-blindness

* Congenital pterygium or epitarsus is an abnormality of the eye in which there is a fold in the conjunctiva or membrane lining the eyelid and covering the front of the eyeball. It is described as due to growth of the sclera over the cornea. This may continue until the pupil is covered, causing blindness. If removed by operation, the growth will recur.

was common in the Middle Ages, and is recorded on an Egyptian papyrus, 1500 B.C. That the inheritance of night-blindness was recognised as early as 1774 is stated by Dr. J. Bell (1922), who gives a number of pedigrees. There are certain cases in which a normal son of an affected father appears to transmit the disease, but they are so few that they evidently require a special explanation. In those pedigrees in which night-blindness is recessive, myopia is frequently associated as a sex-linked condition in the same males who show night-blindness.

Miss J. Bell points out that "Nasse's law" (male sex-linked inheritance) holds not only for night-blindness but also for pedigrees of hæmophilia, pseudo-hypertrophic muscular paralysis, nystagmus, Leber's disease, megalocornea, colour-blindness, etc. She says (p. 29): "We can find no common factor in these conditions which might offer any clue to the explanation of their common mode of descent." The clue, of course, is that they all follow the path of an X chromosome in descent, and must therefore result from different pathological genic changes in that chromosome.

It is pointed out from the pedigrees that 24 daughters of unaffected sons—*i.e.*, 86 per cent.—transmit; and Dr. Bell thinks that with fuller information this percentage would be reduced. But *all* daughters of affected males may be expected to transmit to half their sons, because all have received a defective X chromosome from their father. In small families, however, only normal sons may appear, and yet the mother may be a transmitter.

Extensive pedigrees of night-blindness (hemeralopia) running into five, six, or even eight generations are published by Varelmann (1925), with many clinical details. He also finds it to be a recessive (male) sex-linked character. In an analysis of the pedigrees he finds that when the father is affected and the mother normal, 38 of the sons are normal and 4 affected (the latter presumably because their mother was a transmitter); of 23 daughters, 21 were shown to be carriers. Of the 154 sons from normal fathers and carrier mothers, 53 were normal, 93 affected; hence a large excess of abnormal sons.

Retinitis Pigmentosa.—The most elaborate study of retinitis pigmentosa and allied diseases is that of Dr. Julia Bell (1922). It is a developmental defect, usually but not always accompanied by night-blindness as a symptom. Nettleship included, as allied conditions, retinitis pigmentosa sine pigmento (described by Leber in 1871), retinitis punctata albescens, gyrate atrophy of

the choroid and retina, choroideremia, and two types of congenital stationary night-blindness. Retinitis pigmentosa is characterised by its progressive nature, leading to blindness, and by its contracted vision, causing the patient to peer around. Its onset is usually before twenty, and it may even be congenital. Pigment is deposited along the bloodvessels, and blindness frequently supervenes before forty. In certain pedigrees it is congenital, in others invariably late, still others show a very rapid course. It is uncertain whether the progressive degeneration leading to blindness arises in the layer of the choroid which is responsible for nutrition of the retina, in the rod and cone layer of the retina itself, or in the retinal bloodvessels along which pigment develops.

Many pedigrees of retinitis pigmentosa are free from other defects. Dr. Bell states that out of a total of 919 individuals, 656 taken from 329 sibships have no other defect noted. In 96 cases it was associated with deafness or deaf-mutism. These may be aspects of a common cause, or the association may be due to separate but linked factors. In the pedigrees there are nine cases of polydactyly associated with retinitis pigmentosa, and two cases in the same stocks of retinitis without polydactyly. This suggests that the genes for these two conditions were linked in the same chromosome with crossing-over. A similar relation between retinitis and glaucoma (a disease of the eye with intense intra-ocular pressure, resulting in hardness of the eye and blindness) is suggested by the occurrence of eleven cases of glaucoma with retinitis pigmentosa and two cases of glaucoma alone in siblings.

Dr. Bell assumes (p. 22) that retinitis pigmentosa, when it occurs only once in a pedigree, is not inherited. But this conclusion by no means follows if the condition is recessive in inheritance. It appears more frequently in males, in the ratio 454 ♂ : 363 ♀, or 55·6 per cent. The large pedigrees show that it is usually inherited as a simple dominant, DR × RR matings sometimes giving a considerable preponderance of affected individuals, but is recessive in some pedigrees. Rarely in a pedigree showing dominance a generation may be skipped. Quite possibly the dominant and recessive types may differ in minor symptoms, such as time of onset. Clearly, in dealing with the subject statistically, the two types of pedigrees should not be lumped together. In Nettleship's pedigree it is sex-linked.

The allied condition of retinitis punctata albescens, in

which white dots appear in the fundus, is evidently from the pedigrees a recessive, since it commonly occurs in cousin marriages.

Choroideremia is a very rare developmental defect in which the choroid may be entirely absent. The eleven small pedigrees by Dr. Bell show that it usually occurs in single cases or in two sibs from normal parents. Hence it is probably a recessive. It often occurs in pedigrees showing other ocular defects, including retinitis pigmentosa and stationary night-blindness.

Gyrate atrophy of the choroid and retina is extremely rare. Its symptoms are night-blindness, defective vision, and contraction of the visual fields, with or without pigmentation of the blood-vessels. The pedigrees indicate that it is also recessive.

Beckershaus (1925) concludes that all diseases causing retinal degeneration are generally recessive. But he himself points out cases of inheritance of retinitis pigmentosa as a dominant through three, four, five, and six generations. He endeavours to explain the change from recessiveness to dominance by the application of Plate's theory of a basic factor supplement. Wibaut (1927), from a study of retinitis pigmentosa in Holland, finds an infrequent dominant form, and concludes that there are possibly a number of unrelated recessive forms, each determined by its own inheritance factor. Mann (1928) has studied a family in which retinitis pigmentosa was combined with *Leber's disease*, or *hereditary optic atrophy*, a form of retrobulbar optic neuritis, which also causes rapid failure of vision. The latter is usually inherited as a sex-linked recessive—*i.e.*, like hæmophilia—as Leber showed in 1871. A family of six boys and two girls from a cousin marriage all had retinitis pigmentosa. A sister of the mother of this family had five children, two of which showed Leber's atrophy and one perhaps the beginning of retinitis pigmentosa.

Nettleship (1909) found that Leber's disease could occur in women. When both mother and father have it, all the sons and half the daughters will be affected, and the other daughters will transmit it. He also found that two normal parents may have an affected daughter and that an abnormal daughter may have normal sons. In the Nettleship pedigrees, twelve families from affected ♀ × normal ♂ gave 64 children, 33 normal : 33 affected (1 : 1), and of the latter there were 21 ♂ and 12 ♀. Transmitter ♀ × normal ♂ gave 215 children, 150 normal : 65 affected.

Macklin (1927) cites a pedigree of Worton in which he

concludes that the transmission is not according to the "law of Nasse" but according to that of Lossen. According to the former, in such male-sex-linked inheritance as that of optic atrophy or hæmophilia, transmission takes place not only from carrier mothers to their sons but also from affected men to the sons of their daughters; while "Lossen's law" would say that *affected men do not transmit*. Much unfruitful discussion has been based on this supposed inability of affected men to transmit their defect. Apart from its improbability on biological grounds, the idea appears to have grown up because hæmophilic sons usually die before they are old enough to reproduce. In

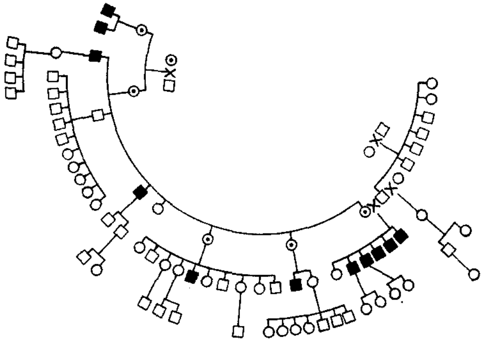


FIG. 19.—PEDIGREE OF OPTIC ATROPHY (LEBER'S DISEASE). (After Vogt.)

the above pedigree of optic atrophy, only three affected men have children. Eight of the latter are girls, but none of them have yet had children. Most, at least, of the pedigrees which are supposed to show failure of the male to transmit are subject to the same criticism.

A typical pedigree of Leber's disease, showing its sex-linked character, confined to males and transmitted by females, is seen in Fig. 19, taken from Vogt (1922). Pines and Tron (1925) cite a case where five brothers in a family of thirteen were afflicted. Their mother's brother was also affected. The onset of the disease began in the uncle at twelve years of age, and in the five brothers at the ages respectively of 28, 20, 14, 31, 31.

Schönenberger (1926), in reviewing the subject, brings together 127 pedigrees by 16 authors. Of those affected, 534 are ♂ to 99 ♀. In some of the pedigrees no female has it, in others they often have it. It may also appear at different ages, so that different conditions may be represented. None of these pedigrees show whether a man can transmit through a normal daughter to his grandsons. In one pedigree a female is affected, as well as her brother. This may be a case of variable dominance. Again, more than half the daughters of affected fathers appear to be transmitters. The same appears to be true of degeneration of the macula lutea. Kawakami (1926) also finds the condition following the X-chromosome in his pedigrees, but some heterozygous females showing it. The age of onset of the disease varies, as does also its occurrence in different races, the Japanese exhibiting it most frequently. It has no relation to the age of puberty. Usher (1927) describes a family with 16 cases in 6 generations, and another with 8 cases in 5 generations. There is said to be no consanguinity of the parents in either pedigree, but in both the inheritance is that of a recessive.

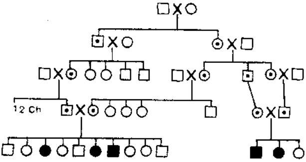


Fig. 20.—Recessive Ophthalmoplegia. (After Waardenburg.)

Ophthalmoplegia, which is due to paralysis of certain muscles moving the eye, has been traced as a congenital condition in several pedigrees, in some of which it is confined to the males, while in others it appears as an ordinary dominant. Waardenburg (1924*a*) describes a recessive form which suddenly appeared (Fig. 20) in five individuals of the fifth generation descended by intermarriage from a common pair of ancestors, both of whom were presumably carriers. There are two forms, ophthalmoplegia externa and interna, depending on which muscles are paralysed.

Defects of the iris and the lens of the eye furnish a large proportion of the inmates of blind schools. When the inherit-

ance of these conditions is understood by doctors and patients there should be a slackening in the serious increase of blindness through inheritance, for those who would transmit blindness should obviously be advised to refrain from reproduction.

Aniridia, or absence of the iris, has been described in several pedigrees cited by Macklin (1927). According to Clausen, there is always a trace of the iris remaining. Cunningham records aniridia in four generations of a family, where it appears to be a simple dominant but skipped one generation. In various pedigrees it is combined with other eye defects. In that of de Beck, coloboma and aniridia were interchangeable, a parent with one condition having children with the other, and the same happened in two other pedigrees. Sedgwick (1861) described cases of the inheritance of aniridia.

Risley (1915) describes a family in which the mother was normal and the father had double aniridia. They had 13 children, all with double aniridia. Of the 63 grandchildren (32 ♂, 31 ♀) at least 61 showed the defect, while in the fourth generation at least 39 out of 42 had it. Thus 96 per cent. of the descendants in this remarkable pedigree were aniridious. From the way the results are stated, it is impossible to draw conclusions regarding the manner of inheritance. Were the various spouses normal or aniridious, and was there inbreeding? It is to be hoped that another generation of medical practitioners will know enough about heredity to be able to state the essential facts when they undertake to publish a pedigree of this kind. Duggan and Nanavati (1927*a*) cite a case where all four children of a third wife were affected, the previous children of the father being free. The mother had nystagmus, bad sight, and probably aniridia.

Retinal detachment is another condition which is inherited when it is not due to an injury. According to Macklin (1927) it appears to be a dominant in some pedigrees, recessive in others, and male-sex-linked or diagynic in still others.

Glioma retinæ (Bell, 1922) is extremely rare as an inherited condition. It has various names, and until recent years was almost invariably fatal at a very early age. Now early operation leads to recovery, although it involves the loss of one or both eyes. Such blind people are allowed to marry, and they frequently transmit the defect to their children. A tumour-like growth takes place from the retina, possibly due to misplacement of retinal cells during fœtal life, these cells multiplying to form a parasitic growth. Dr. Bell cites 128 cases in 36 small pedigrees.

It may be congenital, rarely develops after seven years, and is not associated with other defects. The pedigrees show that it frequently develops in children of normal parents, but that it may also be transmitted directly from mother or father to children. It occurs in both sexes, and the method of inheritance is not clear, but it may be a recessive. Clausen (1925) collected cases from the literature, showing sibships with 83 affected: 61 unaffected children. Mohr (1926) finds it to be lethal in the homozygous condition.

Colour-Blindness.

Numerous pedigrees of colour-blindness are now on record. Red-green colour-blindness is generally inherited as a typical male-sex-linked character, recessive in the female, due to a gene in the X chromosome.

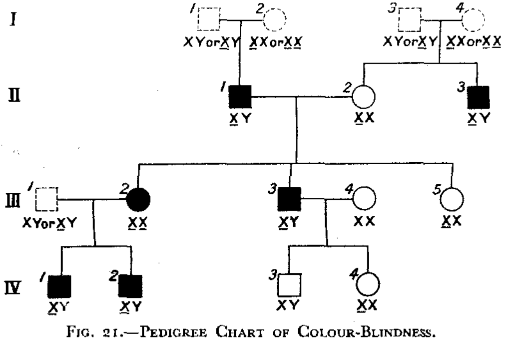


Fig. 21.—Pedigree Chart of Colour-Blindness.

An early record of sex-linked colour-blindness ("Daltonism") is of much interest. It was communicated to the Royal Society in 1778 by the Rev. Michael Lort, and consists of a letter from Mr. J. Scott to the Rev. Mr. Whisson, of Trinity College, Cambridge, describing his infirmity and stating which of his relatives also possessed it. This has been thrown into the form of a pedigree chart by Cole (1919), from whom Fig. 21 is taken with modifications. No. III. 3 is the deponent, and it

will be seen that his father and his mother's brother were also colour-blind. His mother, though normal, had a colour-blind son and daughter, and she must therefore have been heterozygous for the character (see Fig. 8, p. 23, which gives the history of the sex chromosomes). Homozygous colour-blind mothers transmit the defect to *all* their sons, as in generation IV., while normal but heterozygous mothers transmit it to half their sons.

Fathers, on the other hand, never transmit the defect to their sons; but half their daughters by normal mothers will, though normal, be transmitters to half *their* sons by a normal father. Heterozygous mothers with a colour-blind father will have 50 per cent. of colour-blind daughters (while all the daughters will transmit the defect), and half the sons of such a marriage will also be colour-blind. Regarding the deponent's grandparents there is no record, but the grandmothers must both have been either colour-blind or heterozygous transmitters of the defect, while the grandfathers may or may not have been colour-blind.

A shorter account of another case of colour-blindness is given in a letter written in the previous year by Mr. Joseph Huddart to the Rev. Joseph Priestley, and published in the *Phil. Trans.*, 1777. A shoemaker named Harris from Maryport, Cumberland, was colour-blind, having discovered it at the age of four years through being unable to distinguish a red stocking from an ordinary (presumably black) one. He also observed that "when young, other children could discern cherries on a tree by some pretended difference of colour, though he could only distinguish them from the leaves by their difference of size and shape." Colour-blindness consists essentially in the failure to distinguish red from green. This man "had two brothers in the same circumstances as to sight; and two other brothers and sisters who, as well as their parents, had nothing of this defect." Evidently the mother was heterozygous, and transmitted the defect to half her sons. According to Bateson (1913), in European countries at least 4 per cent. of the male population and less than 0·5 per cent. of the females are colour-blind. Howell (cited by Macklin, 1927) states that only 0·01-1 per cent. of females show it, but 2-4 per cent. of males.

Bowditch (1922) describes three families related through marriage, all showing the usual type of sex-linked inheritance. In one of the families the condition is present in the males of three generations, being transmitted in one case through two

generations of females before reappearing in a male. In the second family there were two cases of colour-blind females, one of whom had three sons, two of whom were known to be colour-blind.

Little and Gibbons (1921) have considered the inheritance of hæmophilia and colour-blindness in relation to the presence of sex-linked lethal factors, which would, of course, follow the same line of inheritance. If there is linkage between a sex-linked lethal factor and the normal allelomorph to hæmophilia or colour-blindness (the latter being due to different defects in one X chromosome, and the normal to a non-defective X chromosome), then the authors show that there should be an excess of abnormals among the males in pedigrees in which these

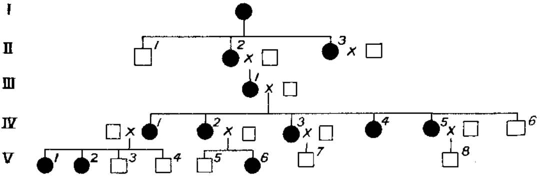


FIG. 22.—PEDIGREE OF FEMALE SEX-LINKED COLOUR-BLINDNESS.

sex-linked diseases occur, and a decreased proportion of females in families in which an excess of affected males does not occur. From the data of Bulloch and Fildes (1910), as well as other data at the Eugenics Record Office, they find these expectations fulfilled, thus furnishing evidence of sex-linked lethal factors in man.*

A remarkable case of female-sex-linked inheritance is described by Cunier (1839), in which colour-blindness is inherited from mother to daughter alone through five generations (see Fig. 22) in a Belgian family. This again appears to be because the character is behaving as a dominant instead of a recessive. The condition is transmitted from mother to

* Lethal factors have been most extensively studied in *Drosophila*. Their presence causes the normal development to go astray, leading to the death of the organism at an early or a later stage in its development. Enriques (1919) has shown that in the fly *Calliphora erythrocephala*, certain individuals produce 25 per cent. of non-vital offspring. The larvæ cease to eat after two or three days and then die. Some of the non-lethal offspring in turn produce lethals in varying proportions.

daughter directly in the female line—that is, it is sex-linked or, better, *female-sex-linked*. It may be spoken of as *matrilineal* in descent. The appearance of the character in heterozygous females shows it to be a dominant. We may think of such females as having one affected and one normal X chromosome. This would be transmitted to half the sons, none of whom are affected, presumably because the presence of the Y chromosome in some way neutralises its activity.* Half the sons should then be capable of transmitting colour-blindness to all their daughters. Unfortunately the records of the family furnish no data regarding the male lines of descent in this family. But it seems likely that if such transmission had occurred it would have been noticed, because the facts are evidently carefully recorded. It is possible, therefore, that transmission through the males may fail, just as it appears to fail to be inherited through two successive generations in the female line in the night-blind family studied by Newman (1913) (see p. 74). Another possible explanation would be that only sons who have received a normal X chromosome are viable. This should lead to a deficiency of males in the offspring. It is very interesting to find colour-blindness transmitted as a sex-linked dominant in this family, and a sex-linked recessive in others. In this Belgian family Madame Th—— (III. 1, Fig. 22) and her aunt and grandmother could not distinguish blue from red ("rouge"), while her descendants confounded blue with "cerise." The eyes of affected individuals were very sensitive to light.

Sedgwick (1861) states that inability to distinguish colours is often associated with inability to distinguish sounds, and cites a family in which all the colour-blind members were also stone-deaf. Of historical interest is the paper by Pole (1893). Some important work of the last few years may now be cited.

Vogt (1922) gives a pedigree (Fig. 23) in which two red-green colour-blind stocks have intermarried and produced a colour-blind daughter. He recognises four conditions in red-green colour-blindness: *protanopia* = red blindness, deuteranopia = dichromacy, protanomalia = "green-sightedness," and deuteranomalia = "red-sightedness." Female dichromacy can then arise (1) from a carrier × a dichromatic male, or (2) from a dichromatic female × a dichromatic male. In the G. family

* There is some evidence (see p. 27) that in man and in fishes, unlike insects, the Y chromosome plays an active rôle in inheritance.

(Fig. 23), I. 5 and IV. 2 both had protanopia, III. 4 deuteranopia. Hence protanopia is dominant to deuteranopia.

In the Hu family (Fig. 24), Vogt and Klainguti (1922), again two families carrying dichromacy have intermarried. I. 2 and I. 4 must have been conductors, and I. 3 must have been colour-blind, although there is no record of his condition. II. 7 × II. 8 represents the cross $\underline{X}Y \times \underline{X}\underline{X}$. Hence all the

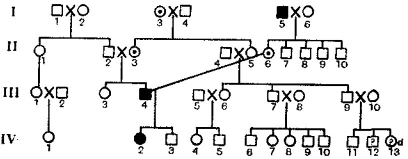


Fig. 23.—Pedigree of Colour-Blindness (Dichromacy). (After Vogt and Klainguti.)

children would be colour-blind. In the third generation the children marked with a ? were too young to be tested. In five families studied, female dichromacy came from a carrier marrying a colour-blind man, in addition to the above marriage between two dichromatics. It was not fully determined how protanopia and deuteranopia behave when crossed together.

Danforth (1924), basing his calculation on the statistical frequency of 4 per cent. colour-blind males and 0·4 per cent.

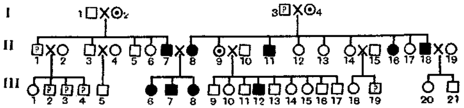


Fig. 24.—Colour-Blindness—the Hu Family. (Vogt and Klainguti.)

females found by Vogt in Central Europe, shows that only 0·16 per cent. of the females should be colour-blind if the sex-linked rule is strictly followed. There is no present explanation of the excess of colour-blind women over expectation.

Waaler (1927) has made an important contribution to the subject by careful testing of 18,121 school children in Oslo. He recognises the four conditions of Professor Vogt in red-green colour-blindness. In any given pedigree usually only one kind

of colour-blindness was found. Each of these four types then has its special gene in the X chromosome. The four types are also found in women, the homozygous woman being phenotypically the same as the heterozygous men in her pedigree. The factors for protanopia and protanomaly are allelomorphs, the latter being dominant. Similarly, deuteranopia and deuteranomaly are another pair. It is somewhat uncertain whether these two pairs are allelomorphic to each other or lie in different loci of the same chromosome. But four women with the factors for protanopia and deuteranomaly have normal sight. Hence probably all factors are in the same locus.

Since these different types of colour-blindness exist, if a normal woman has a colour-blind son, one cannot assume that she transmits a *single* factor for colour-blindness. One must also know that she has also normal sons or a normal father. Also if one parent has protanopia or protanomalia, and the other deuteranopia or deuteranomalia, then none of the daughters might be colour-blind, although both parents were. But such a case is not actually known. It was found that normal is not fully dominant over deuteranomaly, and that protanomaly and deuteranomaly are probably not fully dominant over protanopia and deuteranopia.

In Oslo the frequency of colour-blindness was found to be 8-9 per cent.; for girls scarcely 0·5 per cent., and this chiefly deuteranomaly. For boys it was about 1 per cent. each for protanopia, deuteranopia, and protanomaly, and about 5 per cent. for deuteranomaly.

Total colour-blindness, on the other hand, is clearly a recessive character. A careful study of this condition has been made in Switzerland by Peter (1926). A total of 60 families showing total colour-blindness have been described in the literature since 1880. In 14 of these blood relationship of the ancestors was shown. One case was described of an individual with one eye colour-blind and the other normal. The chief symptoms of total colour-blindness are (1) absence of colour sense, (2) photophobia, (3) very bad vision, (4) nystagmus, (5) nyctalopia (seeing best in twilight). In the whole literature scarcely 100 cases of total colour-blindness are known. Professor Vogt collected 13 of these by following up the relatives of children with weak sight. In the 29 families previously recorded the sibships numbered 126 normal : 49 colour-blind. The 8 new families show a ratio of 49 : 16, where 3 : 1 is expected for a simple recessive. Some of the latter pedigrees are very

extensive, being traced back through six or seven generations and large numbers of individuals, all normal except one or two colour-blind in the last generation. Aniridia is also present in one pedigree, and partial colour-blindness in another.

Another case of total colour-blindness is briefly recorded (Baetjer, 1929) in a girl of twenty-two. Her brother, father, and her mother's brother were also colour-blind, but the details of their condition were unknown. This would appear to be a case of the usual sex-linked inheritance, in which half the sons and half the daughters of a colour-blind father and a carrier mother might be expected to be colour-blind.

Macklin (1927) gives a pedigree (Fig. 25) of colour-blindness and a crooked little finger. The original parents were cousins

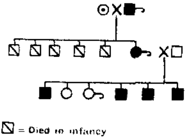


FIG. 25.—PEDIGREE OF COLOUR-BLINDNESS AND A CROOKED LITTLE FINGER. (After Macklin.)

and the mother must have been a carrier. The daughter II. 6 would be homozygous for colour-blindness. She would therefore transmit it to *all* her sons, and all her daughters would be carriers. The crooked little finger is independently inherited as a simple dominant. Halbertsma (1927) describes a family with recessive sex-linked degeneration of the macula lutea together with colour-blindness. Some members of this family had only colour-blindness, without dark pigmentation of the retina.

Maculo-cerebral degeneration is a condition which begins at seven to twelve years and is frequently, but not uniformly, fatal. Macklin (1927) gives several pedigrees, from which it appears to be a recessive, but the evidence is inconclusive. The closely allied condition, *amaurotic family idiocy*, is a rare disease, reported almost exclusively in Jews, especially Russian Jews, but known to occur in Gentiles, possibly when they have Jewish blood. It involves the central nervous system. The infant becomes blind, paralysed, and mentally abnormal, and dies in infancy. It is a recessive in inheritance, appearing from normal parents, and naturally with greater frequency following intermarriage.

Two interesting, because contrasted, pedigrees of *amaurosis*, or hereditary blindness, are given by Sedgwick (1863). In the first (Fig. 26) the condition is apparently confined to the females, who go blind before middle age. In the second the same condition is confined to the males and skips a generation in inheritance (Fig. 27).

Glaucoma, a disease of the eye with intense intra-ocular pressure due to blocking of the lymph drainage canal, whether

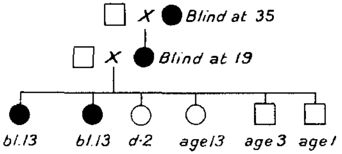


FIG. 26.—FEMALE SEX-LINKED BLINDNESS.

congenitally or by infection, resulting in hardness of the eye and ultimate blindness, is one of the conditions which immigration agents have to diagnose in its early stages. It is relatively rare and is probably generally inherited. James (1927) gives a pedigree with eight cases in two generations, from which it is probably a Mendelian dominant. Some pedigrees also show "anticipation." Kamenetzki (1925) described a juvenile form of glaucoma, which usually manifests itself at puberty

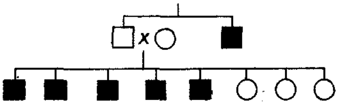


FIG. 27.—MALE SEX-LINKED BLINDNESS.

and was confined to males, while in other forms of glaucoma more women than men are usually affected. The pedigree of Kamenetzki (Fig. 28), from the Russian farming population around Irkutsk, shows the common form of male-sex-linked inheritance. The case of transmission from an affected man through his daughter to a grandson is regarded as doubtful, though there is no reason why it should not occur.

Blue sclerotics is a condition of the sclerotic coat of the eyeball, in which it is a pale china blue, due either to abnormal thinness

or abnormal transparency of this layer. The scleral coat may be only one-third its normal thickness, and it is associated with widespread failure in the development of connective tissue. The frequently associated fragility or *brittleness of bones* (*q.v.*) has been known as osteopsathyrosis idiopathica, fragilitas ossium, and by various other names. In a recent monograph (Bell, 1928) the inheritance of the two conditions is discussed together. Deafness due to otosclerosis is also frequently associated. Blue sclerotics is a disease to which the female is especially liable, and she appears to be "slightly more potent than the male as a transmitter of the defect." In a total of 448 cases, 55·4 per cent. were females. Seventy-three pedigrees

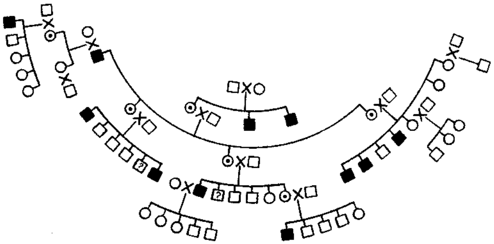


FIG. 28.—SEX-LINKED INHERITANCE OF A FORM OF GLAUCOMA. (After Kamenetzki.)

showing the inheritance of this condition in 463 individuals are given, none of them published earlier than 1903. In nearly all of them a simple dominant factor is indicated, but its occasional sporadic occurrence from ancestors normal for several generations back suggests either a recessive inheritance or a new mutational origin of the condition.

Key (1926) discusses the relation between brittle bones and blue sclerotics. He concludes that blue sclera are the only feature of hereditary deficiency of mesenchyme which is always present and transmitted as a dominant. Idiopathic fragility of bones is due to abnormal development rather than to any metabolic disturbance.

The first history of hereditary blue sclerotics was published by Spurway in 1896, but von Ammon had studied the condition as early as 1841, and it was recognised a decade earlier. It may occur either with or without bone fragility, and in some pedi-

grees fragility of bones is always accompanied by blue sclerotics. Probably the two defects are germinally independent but genetically linked. Of the adults with blue sclerotics, 60 per cent. were also liable to fractured bones, 60 per cent. had otosclerosis, and 44 per cent. had all three defects. Burrows (1911) gives a pedigree in four generations (Fig. 29), of blue sclerotics, accompanied in some by brittle bones. The case of Duggan and Nanavati (1927*b*) is peculiar in some respects. In a Mohammedan family in Bombay the side of the face as well as the affected eye is light blue in colour. The condition is inherited from a grandmother, whose three daughters had it, and the son slightly. The son's three children were normal, while the eleven children (5 ♂, 6 ♀) of the three daughters were all, according to the pedigree, affected. Yet it is stated in the text that only females were affected, except the one male

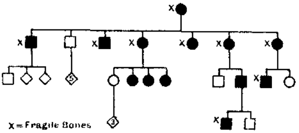


Fig. 29.—Inheritance of Blue Sclerotics and Bone Fragility. (After Burrows.)

slightly. This discrepancy indicates that the pedigree may not be too reliable. There was no evidence of fragilitas ossium or deafness in this family.

Short-sightedness (*myopia*) generally appears as a recessive in inheritance. Clausen (1924) gives many pedigrees and regards it as recessive. Vogt believes it depends on two factors, (1) length of the axis, (2) corneal curvature. Liepin (1924) gives four small pedigrees. From marriages between those who were not short-sighted and had myopic children, the numbers were 166 normal : 52 myopic, which is very close to a 3 : 1 ratio (163·5 : 54·5). When both parents were myopic all the children were so. Hence he concludes it is a simple monohybrid recessive.

Yamazaki (1927) examined 1,906 families of myopic and emmetropic (normal) individuals, and concludes that high-grade myopia is due to two inherited elements. Medium cases of myopia show only 9·2 per cent. of inheritance, whereas high-grade cases show 25·2 per cent. Short sight occurs more often

in the children of high-grade myopics than in those of emmetropics. Czellitzer (1928) has studied this subject extensively, having examined 911 families in Berlin. In DR × RR crosses he finds that less than 50 per cent. are myopic, and in DR × DR less than 25 per cent. Hence he concludes that more than a single factor is involved. He assumes two factors, K and U, myopia appearing in the absence of both—*i.e.*, kuku—and a series of intergrades in the presence of one in the homozygous or heterozygous condition. There is no tendency for the first child to be myopic, as some have claimed, nor does the age of the parents have any influence.

Unfortunately, Czellitzer gives no pedigrees, but his treatment is purely statistical. Based on his two-factor hypothesis, there would be nine types ranging from normal (KKUU) to highly myopic (kkuu), and crosses between these types would give ratios (normal: myopic) ranging from 15 : 1 to 3 : 1 or 1 : 1. The results appear to be statistically in good agreement with his hypothesis, but it can only be satisfactorily tested by the examination of many pedigrees. Perhaps there is a main recessive factor for myopia, with one or more modifying factors which affect its intensity.

Strabismus, or squinting, is often due to defective musculature of the eye, and is stated by Sedgwick (1861) to be hereditary in some families for many generations. In one family the five boys squinted in the left eye or in both eyes, while the five girls were normal. Their father and mother were normal, but the mother's sister had a boy and a girl both squinting with the left eye.

Czellitzer (1923) has studied the inheritance of squinting in 306 families with 365 squinting children in Berlin. Cohn found among 10,060 school children 222, or 2·2 per cent. of squinters. Among sibs numbering 891, Czellitzer found 140 cases, hence 15·4 per cent. Inward and outward squinting are distinguished. He concludes that the condition is recessive, but not due to a single factor, and he finds it more frequent in women (54·5 per cent.) Baur, Fischer, and Lenz (1927) give a pedigree from Vogt indicating a recessive inheritance, and another from Clausen and Bauer where it is clearly dominant. Macklin (1927) cites pedigrees in which it is recessive, and another in which it is dominant, while Clausen (1924) finds in still others that it is due to the presence of several factors. Man is, I believe, the only species in which the same character may behave as a dominant in one pedigree and a recessive in

another. This condition can now be recognised as fairly common in the human species, and it requires a special explanation. It is known that in certain genera of plants "doubling" of the flowers is a dominant, while in others it is recessive to normal, but so far as known there is constancy in the type of inheritance in any one genus or species.

Hyperopia, or long-sightedness, Clausen (1924) considers to be recessive, but in some pedigrees it is clearly a dominant. The condition is less well defined than myopia, either as a defect or in inheritance. There are many grades of hyperopia, as there are of myopia, and it is not known whether myopia × hyperopia will give a normal eye. It is important that observations should determine this point.

Astigmatism (a defect in the lens of the eye, in which not all rays are brought to a focus at the same point) is undoubtedly inherited in many pedigrees. According to Macklin (1927) the axis and degree of astigmatism are the same in all affected members of a family, and the inheritance is probably that of a dominant.

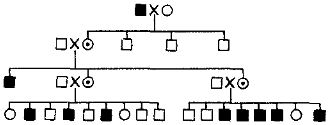


FIG. 30.—HEREDITARY NYSTAGMUS. (After Holm.)

Nystagmus (continuous rolling movement of the eyeball) appears to be usually a dominant character, although it may skip a generation. Nettleship gives a sex-linked pedigree. Holm (1926) points out that in certain pedigrees it is a simple dominant, while in others it is confined to the sons but transmitted by the daughters. At least eleven pedigrees of the latter type have been published, and some partly follow this type. Both the dominant and the sex-linked type are alike in their symptoms: shaking of the head, astigmatism, and weak eye pigmentation (partial albinism). It should be considered as due to a defect in the development of the eye, causing amblyopia (dim sight). Holm gives two pedigrees, both sex-linked. One (Fig. 30) has 10 cases in four generations, the other 7 cases in three generations.

Megalocornea is an interesting condition, in which the eyeball

is abnormally large. This may result from glaucoma (hydrophthalmus) in childhood, but is usually an independent abnormality accompanied by very good sight. It cannot therefore be regarded as a defect. Kayser (1914*a*) gives a family pedigree with 16 cases in five generations. It was found only in males, and except in one case it was not inherited direct from father to son, but through normal daughters of affected fathers, hence ordinary male-sex-linked. Kayser (1914*b*) describes another family with 17 cases in six generations, the inheritance being through sound mothers to half their sons. Grönholm (1921) gives another pedigree with the same type of inheritance, but this includes a marriage between a woman transmitter and a man with megalocornea. They have two daughters affected and one normal son. This is in accordance with expectation for $\underline{X}X \times \underline{X}Y$. Finally, Gredig (1926) describes a family in which the condition is inherited as an ordinary Mendelian dominant, with 13 occurrences in four generations. He, like earlier authors, points out the difficulty in distinguishing megalocornea from hydrophthalmus.

Microcornea, the opposite of megalocornea, is rare. The pedigrees of this condition are small and the manner of its inheritance uncertain. *Keratoconus* is another rare deformity of the cornea, and may cause blindness. It is probably recessive, but may be due to the presence of independent factors.

Ectopia lentis, or congenital dislocation or displacement of the lens, is a condition which occurs in various degrees and interferes more or less with vision. Vogt (1905) described a family in 18 members of which spontaneous dislocation of the lens took place during middle age (twenty to sixty-five years) and was inherited as a dominant. Fifteen out of 30 males (50 per cent.), but only three out of 26 females (12 per cent.), showed the condition, and the latter did not transmit. Waardenburg (1924*b*), in a study of these conditions, distinguishes ectopia pupillæ, ectopia lentis congenita, ectopia lentis et pupillæ, and ectopia combined with other abnormalities. Usually ectopia of the pupil is unilateral and uninherited. Waardenburg gives a pedigree showing 15 persons in four generations with bilateral ectopia. The inheritance is that of a simple dominant, and this is usual in other pedigrees. The direction of the displacement is always upwards and inwards, but it occurs in grades from scarcely abnormal to the largest displacement. Usually also the pupil is narrow, there are structural changes in the iris, remains of the membrana pupil-

laris, and absence of the limbus. The condition is independent of iris colour. Ectopia lentis is also found to be recessive in three other families.

Cameron (1926) describes hereditary dislocation of the lens in four generations (Fig. 31). Fourteen persons are affected, only one a male. Both lenses were dislocated in every case, the vision was seriously affected, and a squint (convergent or divergent) was apparent. Five members had to be trained in an institution for the blind. The condition was female-sex-linked with the one exception. Fecht (1927) describes luxation of the lens in three brothers and a sister. The parents were normal, as were the next generation from marriages with normals. Evidently the condition was recessive in this pedigree.

Ptosis (drooping of the eyelid owing to paralysis of its muscles) is a condition of which there are many pedigrees, and it is often associated with EPICANTHUS. It occurs in all grades, sometimes only producing a sleepy appearance, but in others

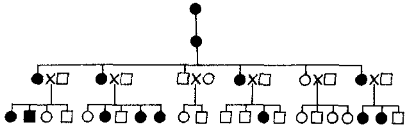


FIG. 31.—HEREDITARY DISLOCATION OF THE LENS. (After Cameron.)

the head has to be thrown back to see. It is not always inherited, but may be caused by an injury or by paralysis of the third nerve. It is due to absence or impairment of the levator palpebræ superioris which raises the eyelid. Usually at least, it is dominant in inheritance. One case is cited by Macklin (1927) of a man with normal parents who had four children showing ptosis. This might be explained by a mutation, or more probably as indicating that the condition was recessive in this pedigree. Briggs (1918, 1919) describes a pedigree of six generations from a woman having this defect. The lineage belongs to a family in the mountains of the Southern States, and includes 128 individuals, half of whom have the defect. Photographs are given, and a chart indicating that the character is dominant. Fhieringa (1924) describes a family in which the mother was unable to lift the eyelids very far. Her ancestors were quite free from the condition so far as could be traced, as was also the father and his ancestors. Yet all the children of

both sexes exhibited the defect. This would appear to be a *de novo* origin of ptosis and its inheritance as a dominant in the children. Weissenberg (1927) gives a pedigree showing ptosis on the left side only, inherited as a dominant in three generations of a Russian family in Baku.

A pedigree combining epicanthus with ptosis was described by Usher (1925). He distinguishes (1) epicanthus supraciliaris bilateralis, in which the skin fold originates in the eyebrows and extends down towards the tear sac or the nostrils, (2) E. palpebralis, the broadest form, and (3) E. tarsalis, which originates in the tarsal fold of the upper lid and loses itself in the skin close to the inner canthus. Such a fold, uniting the upper and lower lids at the inner angle of the eye, is normal in the Mongolian race and occurs with varying frequency in related races. Epicanthus is stated to occur in about half the cases of Mongolian idiocy. It is present in all races in fœtal life, and minor degrees of it are common in infants. It is similar to the plica marginalis of Mongoloids, but is not due to a flat nose. Evidently in adults it represents a failure to complete development. In only one pedigree does epicanthus apparently occur without ptosis. In Usher's pedigree a man with both had 17 similar cases in his descendants in three generations. The inheritance is that of a Mendelian dominant, except in one case where it skipped a generation and another in which two generations were skipped, but the individual in the former case had ptosis on one side only, and in the latter case (IV. 4) epicanthus without ptosis. This pedigree then appears to show two dominant factors closely linked in the same chromosome, with possibly crossing-over in IV. 4. Usher has collected 14 other pedigrees from the literature, in which about 80 cases of epicanthus occur. In only one family is a generation skipped, a normal sister of two brothers with epicanthus having nine children, four of whom had epicanthus.

Manson (1928) cites a family in which the father, two daughters, and a son have epicanthus with ptosis, one girl being normal. They have to throw back their heads or raise their brows to see. A similar family, known as the slit-eyed people, and probably with a combination of epicanthus and ptosis, is described from the mountains of Georgia (Stuckey, 1916). Its members in four generations had constricted eyelids. The manner of inheritance indicates a segregating dominant character.

Reference may be made to certain other conditions of the

eyelids. Peters (1918) records a minor defect in which the lower lids are dark owing to dilated venules and yellowish pigment beneath the skin. This condition was dominant, occurring in 20 individuals of a family in five generations.

Distichiasis, or a double row of eyelashes on each lid, is probably dominant, and at least four pedigrees have been reported. Macklin (1927) cites also lack of eyelashes in father and son, also relaxation of the eyelids due to atrophy of the underlying connective tissue, a dominant in four generations of a French family, and fat hernia of the lids in a mother and daughter in Germany.

Cataract and its inheritance is the subject of an extensive literature in ophthalmological and medical journals. There are many types, all with strong evidence of inheritance. Extensive pedigrees of cataract were collected by Nettleship (*cf.* Bateson, 1913), usually showing dominance. Harman (1910) classifies cataracts as lamellar, axial, stellate, and polar He gives details of a number of pedigrees of inheritance, but no attempt is made to draw conclusions regarding the manner of inheritance. In another paper, however, the same author (Harman, 1909) cites a pedigree of five generations showing the condition to be a Mendelian dominant. Parents who are normal have only normal children. Of fifty-five persons, nineteen were known to be affected. Others who were not examined probably had the defect slightly. Among forty-one persons personally examined or certified, nineteen were cataractous. This is very close to the expected 50 per cent.

Detlefsen and Yapp (1920) describe a case of congenital cataract in cattle, which they conclude behaves as a simple Mendelian recessive. A registered Holstein-Friesian bull inbred with his own stock gave a number of cataractous offspring. There is no record of cataract in any of the ascendants. To unrelated cows this bull produced only normal calves. But thirty-two F_1 daughters mated to an F_1 son gave sixty-three calves, fifty-five of which were normal and eight had congenital cataract of the stellate type.

Macklin (1927) states that 13 per cent. of the pupils in blind schools are blind through cataract. They should obviously not have children, especially in lines of descent in which the disease is dominant. She cites many pedigrees from the literature, including coralliform cataract by Fisher and by Nettleship, presenile cataract by Davenport and by Nettleship, lamellar by Nettleship, posterior polar by Ziegler and Griscom,

zonular by Derby, discoid or Coppock cataract by Nettleship, Chance, Dorell, senile cataract by Green, Nettleship, Dickey, Brown. In all cases it is a Mendelian dominant, with the type fairly constant in each pedigree. A pedigree of Nettleship showed " skipping a generation " in two cases, but these might have developed cataract in their old age. Lutz (1911) was one of the first to recognise that many ocular abnormalities, including distichiasis, ptosis, coloboma, glaucoma, cataracta senilis, and other forms of cataract are inherited as dominants, and that still others are recessive sex-linked.

Danforth (1914) describes the work of von Szily in mating a cataractous male rabbit with a normal female and finding cataract in the rabbit embryos. It was traced to a group of cells in the lens cavity, which proliferate for a time and then degenerate, setting up degeneration in the surrounding lens tissue. Von Szily also found that in certain chick embryos

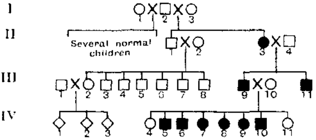


Fig. 32.—Pedigree of Cataract. (After Danforth.)

a fold of the amnion was enclosed in the lens cavity, and this is the probable origin of cataract. Since it is known that the lens of the eye is produced under the stimulus of the optic cup, any aberration in the stimulus might cause a defective lens. In Danforth's pedigree (Fig. 32) the condition appears pretty uniform as lamellar cataract together with defective retina, and is dominant. This pedigree is of particular interest because the original mother of the pedigree was normal, so the condition appears to have originated *de novo*. When cataract is dominant it is strongly so, and if this is a dominant pedigree the condition is unlikely to have been transmitted from ancestors by skipping a generation or more. The original father had several children, all normal, by a first wife, while his second wife, who was also normal, had one cataractous child from which the descent arises. If the condition originated with the father it must have been only in his later germ cells. On the other hand, the second wife may have been responsible for its origin. Nystag-

mus and slight mental deficiency were also noticed in this family. Perhaps the most likely interpretation is, however, that the condition is recessive and was carried by I. 2 and I. 3. Such pedigrees have since been discovered. But on this explanation the large number of affected children in generation IV. is not accounted for unless III. 10 is a carrier. Some cases of lamellar cataract are sporadic and "not inherited."* Danforth points out a tendency for abnormalities to accumulate in a pedigree through the intermarriage of those having different defects. In some cases this tends to the ultimate elimination of the defective stock.

Schmid (1924) produces nine pedigrees of anterior axial embryonic cataract, in which the inheritance is evidently dominant. Knappe (1926) describes 19 cases of perinuclear or lamellar double cataract in a family in five generations. All presented identical ophthalmoscopic pictures. The centre of the lens was filled by black radiating streaks intermingled with fine black spots, and the inheritance is dominant. Romer (1926) gives a pedigree of what Vogt has described as spiess cataract, a very peculiar form of star cataract in which masses of needle crystals are found in irregular groups in the lens. Crystals of other types, including cholesterin, tyrosin, leucin, calcium sulphate, and calcium oxalate, have already been described in the lens. In Romer's pedigree, 10 of the 42 members were affected, and the inheritance was dominant.

Garfunkel (1926), in a study of senile cataract, points out that it can be traced back to the eighteenth century, but there are difficulties because a man may transmit it and die too young to show it himself. The pedigrees of 29 patients with star cataract were investigated. In 12 of them the condition accumulated in the pedigree, and the inheritance was dominant; while in 17 only single cases occurred, and the condition was recessive. Thus the controversy as to whether cataract was dominant or recessive is settled by both types of inheritance occurring in different pedigrees. Only persons reaching sixty years of age are entered in the pedigrees. In the twelve families there were 110 members over sixty years of age. Of these 49 were cataractous and 61 free. Adding to the former 8 others under sixty, we have a total of 57 : 61, which agrees with a ratio of 1 : 1. It is found that cataractous families in

* But it is dangerous to draw this conclusion in relation to a recessive character.

general reach older age than normal families. Khan (1926) gives a short pedigree of dominant lamellar cataract in three generations.

Halbertsma (1928) describes two pedigrees of juvenile cataract. In one, 49 members of a family in three generations have cataract, the principal types being cataracta cœrulea punctata anterior and posterior, perinuclear zonular cataract. In another family near Delft there were 95 persons in the pedigree, and the inheritance was clearly a dominant. In one family in the fourth generation of this pedigree both parents were affected and seven of their nine children. This is in accord with the (3 : 1) expectation where both parents are heterozygous. Another fourth generation family with one parent affected had seven children, all affected. This is probably only the chance departure from a 1 : 1 ratio. Manson (1928) gives another pedigree in which congenital lamellar cataract is inherited as a dominant with 17 cases in four generations. The same pedigree shows 3 cases of a digital abnormality, the little fingers being bent outwards at the lower joint. The eye colours of the members of this pedigree were also examined. Of the cataractous, 7 had brown eyes, 2 grey with brown around the pupil, 4 grey =9 : 4. Of the 12 with normal lenses, 3 had brown eyes, 2 grey with brown around the pupil, and 7 grey (including 1 light blue) = 5 : 7. Hence there was no connection with lack of eye pigmentation, and probably no linkage between cataract and eye colour.

Folkar (1909) traced *nodular opacity of the cornea* through three generations, finding 9 cases abnormal to 19 normal or unknown. Corneal opacity is due to various causes, and is inherited as a dominant in various pedigrees. Opacity of the corneal margin, known as *arcus juvenilis* or embryotaxon, was inherited in Clausen's pedigree in four generations as a dominant, occurring in 21 out of 32 members. Froelich (1924) has studied *flocculus formation* in the iris. This consists in the formation of leaf-shaped or wart-like excrescences on the pigmented pupillary border. The condition is normally found in horses, but is lacking in dogs, pigs, and cats, and is very occasionally found in men. Probably the condition in man is different from that found in animals. Several pedigrees are given, showing that it usually occurs in the males, but is not a simple sex-linked factor. The question remains open whether flocculus formation is due to two or more independent or coupled factors, one or more of which is sex-linked.

Microphthalmus is a condition in which the eye-ball is so small that vision is subnormal or absent. The defect occurs in varying degrees, with anophthalmus as its extreme form. Macklin (1927) records seven pedigrees in which it is a recessive, born of normal parents. Usher (1921) describes a case where it is dominant, associated with myopia and corectopia (displacement of the pupil) in four generations. In a pedigree of Ash (1922) it is of the usual sex-linked type (Fig. 33). Ash makes the statement that " the male members show no tendency to transmit the disease." This is because none of the affected (blind) males married. Had any of them done so, their daughters would no doubt have been transmitters of blindness to half the males of the next generation. Chr. Thomsen (1915) reviews the early literature and describes families having microphthalmia with or without cataract.

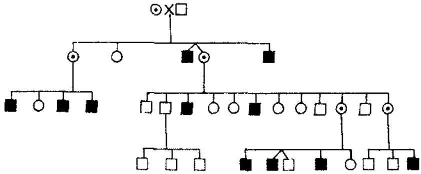


FIG. 33.—INHERITANCE OF MICROPHTHALMIA. (After Ash.)

Microphthalmus is thus a further example of the fact that the same condition may be inherited as a Mendelian dominant or recessive, or as a sex-linked character in different lines of descent.

Hydrophthalmus, or *buphthalmus*, is often used as a term interchangeable with megalocornea. But the latter is always bilateral, while hydrophthalmus is unilateral in one-third of the cases. Also megalocornea is sex-linked, while hydrophthalmus occurs in both sexes, the cornea is less convex, the iris tremulous, and the vision subnormal. The pedigrees are not very extensive, but the condition is probably recessive. *Lagophthalmus* is the opposite of ptosis, in that there is accentuated retraction of the upper lid and inability to close the eyes. According to Macklin (1927), this is caused by various conditions, and is not usually hereditary. But Peters (1915) gives a pedigree showing 5 cases of lagophthalmus in four

generations in direct descent. It is thus a dominant, and that the five individuals were all females may be only chance. *Cryptophthalmus* is a condition in which the lids, which normally separate in the seventh fœtal month, fail to do so. The eye-ball and cornea may also be abnormal. From the evidence of Macklin (1927) it is probably recessive in inheritance.

Coloboma iridis, or congenital fissure of the iris, is inherited. Sedgwick (1861) describes an interesting family, here thrown into pedigree form, having cleft iris. This pedigree (Fig. 34)

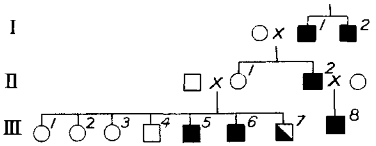


FIG. 34.—FAMILY SHOWING CLEFT IRIS. (After Sedgwick.)

is difficult to explain, for it shows transmission not only as in an ordinary male-sex-linked character, through an unaffected mother to half her sons, but also direct from father to son in two cases, unless the wives here happened to be carriers. One son (III. 7) had the defect in one eye only. Sedgwick also describes inheritance of microphthalmia, absence of eyes, and other ocular conditions.

LITERATURE

ASH, W. M. 1922. Hereditary microphthalmia. *Brit. Med. Journ.*, i. 558-559.

BAETJER, ANNA M. 1929. Case of a totally colour blind female. *Eugenical News*, xiv. 6-7.

BATESON, W. 1913. Mendel's Principles of Heredity. Cambridge Press, pp. 413, figs. 39.

BAUR, E., FISCHER, E., and LENZ, F. 1923. Menschliche Erblichkeitslehre und Rassenhygiene. Munich: Lehmann. 2nd edn., vol. i., pp. 601.

BECKERSHAUS, F. 1925. Dominante Vererbung der Retinitis pigmentosa. *Klin. Monatsbl. f. Augenhlk.*, lxxv. 96-109.

BELL, JULIA. 1922. Retinitis pigmentosa and allied diseases, congenital stationary night-blindness, glioma retinæ. *Treas. of Human Inheritance*, vol. ii, pp. 123, pls. 26.

BELL, JULIA. 1928. Blue sclerotics and fragility of bone. *Treas. of Human Inheritance*, ii. 269-324. pls. 21.

BOWDITCH, H. 1922. Red-green colour-blindness in three allied families. *Journ. Hered.*, xiii. 139-142, fig. 1.

BRIGGS, H. H. 1918. Hereditary congenital ptosis, with report of sixty-four cases conforming to the Mendelian rule of dominance. *Trans. Amer. Ophthal. Soc.*, xvi. 255-276.

BRIGGS, H. H. 1919. Hereditary congenital ptosis, with report of sixty-four cases conforming to the Mendelian rule of dominance. *Amer. Journ. Ophthal.*, ii. 408-417.

BULLOCH, W., and FILDES, P. 1910. Hæmophilia. *Treas. of Human Inheritance*, v. 169-354, pls. 17.

BURROWS, H. 1911. Blue sclerotics and brittle bones. *Brit. Med. Journ.*, ii. 16.

CAMERON, E. P. 1926. An interesting example of hereditary dislocation of the lens occurring in four successive generations. *Brit. Journ. Ophthal.*, x. 384-386.

CLAUSEN, W. 1923-4. Vererbungslehre und Augenheilkunde. *Zbl. f. d. ges. Ophthal. u. ihre Grenzgeb.*, xi. 81-94, 209-218, 417-424, 481-498, figs. 11.

COLE, L. J. 1919. An early family history of colour-blindness. *Journ. Hered.*, x. 372-374, fig. 1.

CRAFT, W. A. 1927. Night-blindness in cattle. *Journ. Hered.*, xviii. 215-216.

CUNIER, F. 1839. Observation curieuse d'une achromatopsie héréditaire depuis cinq générations. *Annales d'Oculistiques*, i. 417-420.

CZELLITER, A. 1923. Wie vererbt sich Schielen? *Arch. f. Rass u. Gesells.-Biol.*, xiv. 377-394.

CZELLITER, A. 1928. Die Vererbung hochgradiger Kurzsichtigkeit (auf Grund einer 27 jährigen Sammelforschung). *Verh. V. Internat. Kongr. Vererb.*, i. 578-594.

DANFORTH, C. H. 1914. Some notes on a family with hereditary congenital cataract. *Amer. Journ. Ophthal.*, 1-12, fig. 1.

DANFORTH, C. H. 1924. The problem of incidence in colour-blindness. *Amer. Nat.*, lviii. 447-456.

DETLEFSON, J. A., and YAPP, W. W. 1920. The inheritance of congenital cataract in cattle. *Amer. Nat.*, liv. 277-280.

DUGGAN, J. N., and NANAVATI, B. P. 1927*a*. A family with aniridia. *Brit. Journ. Ophthal.*, xi. 447-449.

DUGGAN, J. N., and NANAVATI, B. P. 1927*b*. A family with blue sclerotics. *Brit. Journ. Ophthal.*, xi. 445-447.

ENRIQUES, P. 1919. Ricerche sulla eredita della mosche. *Rivista di Biologia*, i. 72-81.

FECHT, W. 1927. Über familiäre Linsenluxation. *Zeits. f. Augenheilk.*, lxii. 162-168.

FLIERINGA, H. J. 1924. Familiäre Ptosis congenita kombiniert mit anderen angeboren Beweglichkeitsdefekten der Bulbusmuskulatur. *Zeits. f. Augenheilk.*, lii. 1-14, figs. 26.

FOLKAR, HERBERT H. 1909. Nodular opacity of the cornea in three generations. *Trans. Ophthal. Soc.*, xix. 42-54.

FROEHLICH, R. E. 1924. Über Flocculus-Bildungen der menschlichen Iris und ihre Vererbung. *Arch. f. Rass. u. Gesells.-Biol.*, xv. 249-262, figs. 7.

GARFUNKEL, B. 1926. Zur Erblichkeit der Katarakta senilis. *Arch. d. Julius Klaus-Stiftung*, ii. 71-78, pls. 5, charts 29.

GREDIG, C. 1926. Eine neue Vererbungsart der Megalocornea. *Arch. d. Julius Klaus-Stiftung*, ii. 79-89, fig. 1.

GRÖNHOLM, V. 1921. Über die Vererbung der Megalocornea nebst einem Beitrag zur Frage des genetischen Zusammenhangs zwischen Megalocornea und Hydrophthalmus. *Klin. Monatsbl. f. Augenheilk.*, lxvii. 1-15, figs. 4.

HALBERTSMA, K. T. A. 1927. Erfelijke ontaarding van de gele vlek gepaard met kleuren blindheid. *Nederl. Tijdschr. v. Geneesk.*, lxxi. 2529-2530.

HALBERTSMA, K. T. A. 1928. Familiare juveniele cataract. *Nederl. Tijdschr. Geneesk.*, lxxii. 855-860.

HARMAN, N. BISHOP. 1909. Congenital cataract: a pedigree of five generations. *Trans. Ophthal. Soc.*, xxix. 101-108.

HARMAN, N. BISHOP. 1910. Congenital cataract. *Treas. Human Inheritance*, iv. 126-166, pls. 8.

HOLM, E. 1925. Myopia from the point of view of heredity. *Acta Ophthal.*, iii. 335-347.

HOLM, E. 1926. Hereditary nystagmus. *Acta Ophthal.*, iv. 20-27, figs. 4.

HOWE, LUCIEN. 1921. A bibliography of hereditary eye defects. *Bull. Carnegie Inst. Washington, Eugenics Record Office*, xxi. 1-45.

JAMES, R. R. A pedigree of a family showing hereditary glaucoma. *Brit. Journ. Ophthal.*, xi. 438-443.

KAMENETZKI, S. G. FRANK. 1925. Eine eigenartige hereditäre Glaukomform mit Mangel des Irisstromas und geschlechtsgebundener Vererbung. *Klin. Monatsbl. f. Augenheilk.*, lxxiv. 133-150.

KAWAKAMI, RIITI. 1925. Über die Vererbung der Oguchischen Krankheit (Eine in Japan vorkommende Form von angeborener Nachtblindheit). *Klin. Monatsbl. f. Augenheilk*, lxxii. 340-349.

KAWAKAMI, RIITI. 1925. Beiträge zur Vererbung der familiären Sehnervenatrophie. *A. von Graefe's Arch. f. Ophthal.*, cxvi. 568-595.

KAYSER, B. 1914*a*. Über den Stammbaum einer Familie mit Vererbung von Megalocornea nach dem Hornerschen Vererbungstypen. *Arch. f. Rass. u. Gesells.-Biol.*, xi. 170-173.

KAYSER, B. 1914*b*. Megalocornea oder Hydrophthalmus? Nebst einen Stammbaum mit 17 Patienten über 6 generationen. Vererbung nach dem Horner-Bollingerschen Vererbungstypus. *Klin. Monatsbl. f. Augenheilk.*, lii. 226-239.

KEELER, C. E. 1926. On the occurrence in the house mouse of a Mendelising structural defect of the retina producing blindness. *Proc. Nat. Acad. Sci.*, xii. 255-258, fig. 1.

KEELER, C. E. 1927. Rodless retina, an ophthalmic mutation in the house mouse, *Mus musculus*. *Journ. Exp. Zool.*, xlvi. 355-405, pls. 3, figs. 4.

KEY, J. A. 1926. Brittle bones and blue sclera. Hereditary hypoplasia of the mesenchyme. *Arch. of Surg.*, xiii. 523-567.

KHAN, W. ALI. 1926. Pedigree of lamellar cataract. *Brit. Journ. Ophthal.*, x. 387-389.

KNAPPE, F. N. 1926. Familial cataract: a study through five generations. *Amer. Journ. Ophthal.*, ix. 683-684.

LIEPEN, T. K. 1924. On the question of inheritance of short-sightedness. (Russian.) *Bull. Bur. Eugenics, Leningrad*, ii. 60-66.

LINA, P. 1927. Zur Kenntnis der Vererbung der totalen Farbenblindheit mit besonderer Berücksichtigung der in der Schweiz bis jetz nachgewiesehen Fälle. *Arch. Julius Klaus-Stiftung*, ii. 143-189, figs. 5.

LITTLE, C. C., and GIBBONS, M. 1921. Evidence for sex-linked lethal factors in man. *Proc. Soc. Exp. Biol. and Med.*, xviii. 111-115.

LUTZ, A. 1911. Über einige Stammbäume und die Anwendung der Mendelschen Regeln auf die Ophthalmologie. *V. Grafe's Arch. f. Ophthal.*, lxxix. 393-437, pls. 4.

MACKLIN, M. T. 1927. Hereditary abnormalities of the eye. II. Inheritable defects involving the eyelids and their mode of transmission. *Canad. Med. Assn. Journ.*, xvii. 55-60.

MACKLIN, M. T. 1927. III. Anomalies of the entire eyeball. *Canad. Med. Assn. Journ.*, xvii. 327-331, 421-423.

MACKLIN, M. T. 1927. IV. Heritable diseases affecting the conjunctiva. *Canad. Med. Assn. Journ.*, xvii. 697-702.

MACKLIN, M. T. 1927. V. Inheritable defects of the iris and lens. *Canad. Med. Assn. Journ.*, xvii. 937-942.

MACKLIN, M T. 1927. VI. Inheritable defects involving the retina. *Canad. Med. Assn. Journ.*, xvii. 1191-1197, 1336-1342.

MANN, IDA C. 1928. Retinitis pigmentosa and Leber's hereditary optic atrophy occurring in cousins. *Ann. of Eugen.*, ii. 77-83, figs. 11.

MANSON, J. S. 1928. Observations on human heredity. London: Lewis, pp. 84, pls. 8, figs. 19.

MOHR, O. L. 1926. Über Letalfaktoren mit Berücksichtigung ihres Verhaltens bei Haustieren und beim Menschen. *Zeits. f. ind. Abst. u. Vererb.*, xli. 59-109, pl. 1, figs. 10.

NETTLESHIP, E. 1909. On some hereditary diseases of the eye. *Trans. Ophthal. Soc.*, xxix., lvii-cxcviii, figs. 69, 110 pedigrees.

NETTLESHIP, E. 1912. A pedigree of congenital night-blindness with myopia. *Trans. Ophthal. Soc.*, xxxii.

NEWMAN, H. H. 1913. Night-blindness. *Journ. Genetics*, iii. 25-38, figs. 2.

OVAZZA, V. E. 1922. *La Stomatol.*, xx. 21-23.

PETER, LINA. 1926. Zur Kenntnis der Vererbung der totalen Farbenlindheit mit besonderer Berücksichtigung der in der Schweiz bis jetzt nachgewiesenen Fälle. *Arch. d. Julius Klaus-Stiftung*, ii. 143-189, figs. 5, pedigrees 7.

PETERS, R. 1915. Angeborener Lagophthalmus in vier Generationen. *Klin. Monatsbl. f. Augenheilk.*, lv. 308-313, fig. 1.

PETERS, R. 1918. Aufflanende Dunkelfärbung der unteren Lider als erbliche Anomalie. *Centlbl. f. prak. Augenheilk.*, xlii. 8-11.

PINES, I. L. JA, and TRON, F. 1925. Hereditäre Neuritis optica (Lebersche Sehnervenatrophie). *Zeits. f. d. ges. Neurol. u. Psychiatrie*, xcv. 762-776, figs. 5.

POLE, W. 1893. On the present state of knowledge and opinion in regard to colour-blindness. *Trans. Roy. Soc. Edin.*, xxxvii. 441-479, pl. 1.

RISLEY, S. D. 1915. Hereditary aniridia. *Journ. Amer. Med. Assoc.*, lxiv. 1310-1312.

ROMER, ALOIS. 1926. Untersuchungen über die Erblichkeit der Spiesskatarakt (Vogt). *Arch. d. Julius Klaus-Stiftung*, ii. 207-220, pl. 1, figs. 4.

SCHMID, C. 1924. Über Vererbung der vordern axialen embryonal Katarakt. *Arch. f. Rass. u. Gesells.-Biol.*, xv. 263-269.

SCHÖNENBERGER, F. 1926. Beitrag zur Kenntnis der homochron-hereditären opticusatrophie. *Arch. d. Julius Klaus-Stiftung*, ii. 59-70, 3 pedigrees.

SEDGWICK, W. 1861. On sexual limitation in hereditary disease. *Brit. and Foreign Med.-Chirurg. Rev.*, xxvii. 477-498, xxviii. 198-214.

SEDGWICK, W. 1863. On the influence of sex in hereditary disease. *Brit. and Foreign Med.-Chirurg. Rev.*, xxxi. 445-478, xxxii. 159-197.

STUCKEY, H. P. 1916. The slit-eyed people. *Journ. Hered.*, vii. 147, pl. 1.

THOMSEN, CHR. 1915. Ueber die Vererbung des Microphthalmus mit und ohne Katarakt. *Klin. Monatsbl. f. Augenheilk.*, liv. 236-249.

USHER, C. H. 1921. A pedigree of microphthalmia with myopia and corectopia. *Brit. Journ. Ophthal.*, v. 289-299.

USHER, C. H. 1925. A pedigree of epicanthus and ptosis. *Annals of Eugenics*, i 128-138, pls. 4.

USHER, C. H. 1927. Two pedigrees of hereditary optic atrophy. *Brit. Journ. Ophthal.*, xi. 417-437.

VARELMANN, H. 1925. Die Vererbung der Hemeralopie mit Myopie. Ein Beitrag zur Vererbung der geschlechtsgebundenen Krankheiten. *Arch. f. Augenheilk.*, xcvi. 385-405.

VOGT, A. 1905. Dislocatio lentis spontanea als erhliche krankheit. *Zeits. f. Augenheilk.*, xiv. 153-165.

VOGT, A. 1922. Über geschlechtsgebundene Vererbung von Augenleiden. *Schweiz. Med. Wochens.*, lii. 77-83.

VOGT, A., and KLAINGUTI, R. 1922. Weitere Untersuchungen über die Entstehung der Rotgrünblindheit beim Weibe. *Arch. f. Rass. u Gesells.-Biol.*, xiv. 129-140, figs. 6.

WAALER, G. H. M. 1927. Über die Erblichkeitsverhältnisse der verschiedenen Arten von angeborene Rotgrünblindheit. *Zeits. f. ind. Abst. u. Vererb.*, xlv. 279-333, figs. 3.

WAARDENBURG, P. J. 1924*a*. Over een recessieven vorm van aangeboren ophthalmoplegie. *Genetica*, vi. 487-492.

WAARDENBURG, P. J. 1924*b*. Over het erfelijkheidsmoment bij de aangeboren verplaatsing van de pupil en van de lens. *Genetica*, vi. 337-382, figs. 14.

WEISSENBERG, S. 1927. Erbliche Nervenkrankheiten. *Arch. f. Rass. u. Gesells.-Biol.*, xix. 425-426.

WIBAUT, F. 1927. Verwantschap, erfelijkheid en de Regel van Lenz bij Retinitis pigmentosa. *Nederl. Tijdschr. v. Geneesk.*, lxxi. 843-847.

YAMAZAKI, Z. 1927. Beiträge zur Vererbung der Kurzsichtigkeit. *Zeits. f. Augenheilk.*, lxii. 49-56.

CHAPTER VI

ALBINISM

THE monograph on albinism in man, by Pearson, Nettleship, and Usher (1911-13) is a very elaborate and detailed treatment, which will serve as a basis for future studies on this subject. It gives not only an elaborately illustrated description of the external features and the histology of the skin and eye pigmentation in albinotic individuals, but also deals with the history of the subject. Pure albinism is a recessive character:* but the condition exists in varying degrees, and its inheritance, like that of so many human qualities, frequently shows complications. Complete albinism occurs in both white and coloured races of man. Pearson divides albinotics into six classes.

Several cases of white spotting in negroes, similar to the classical types seen in paintings in the eighteenth century, have been described in modern times. The evidence certainly, as Pearson (1913) contends, favours the hypothesis that spotting arises *de novo* where a white-black cross or mixed race is crossed back with a pure white or black. In other words, spotting may be considered to arise in certain cases as a somatic segregation, repulsion, or dilution effect, and not to be due to an inherited invisible spotting factor. Striping in various flowers is generally believed to have originated in the same way. A similar case occurred in certain Œnothera hybrids (Gates, 1915). When *Œ. rubricalyx* having dark red buds is crossed with *Œ. grandiflora* having green buds, the F_1 is paler red. If this F_1 generation is crossed back with *Œ. grandiflora*, the colour is further diluted, becoming very pale; and in some families the pattern breaks up into spots, a condition which is inherited.

Once this spotted condition has arisen, it appears then to be fairly stable. Cases of human albinotic spotting are on record which have been transmitted for two to five generations (Stannus, 1913). The condition of spotting has, in some way,

* A recent case in which two complete albino "white" parents had an albino son is illustrated by Davenport (1916).

become stabilised in the germ plasm, and should, therefore, probably be looked upon as a mutation following crossing. Moreover, the spotting in man often follows a characteristic pattern, beginning as a blaze in the forehead, with spotting of the arms, the back largely black, as well as the extremities. Curiously enough, photographs of the Honduras piebald (Pearson, 1913) seem to show an extension of some of the coloured spots as the child develops. The sporadic manner in which spotting appears in all such cases remains to be accounted for. The Honduras piebald had five siblings,* all normal mulattoes. His mother combined Mexican and negro blood, while the father was a pure negro.

In an interesting case recorded by Dr. Stannus and cited in the monograph on albinism, piebaldism was found to occur in five generations of a family of natives at Florence Bay, Nyasaland, appearing in nine individuals. Albinotic patches occurred in the median line, on the anterior half of the scalp, in the epigastric region, and broad "garters" about the knees. The inheritance here extended to the position of the patches.

Seligman (*Lancet*, 1902) describes three albinotic Papuans in three generations of a family. The boy was piebald, with a white blaze in the forehead, white on the abdomen and on the legs from ankles to groin. Stiven (1923) describes an albinotic Sudanese admitted to hospital at Port Said. His father and mother were stated to be typical black Sudanese from Dongola Province, Sudan; his mother's relatives were of normal colouring so far as known, and his father by another wife had black children. This man had one sister who died aged eighteen, and one brother who died aged twelve, both white like himself. His eyes were hazel brown, hair on head and body a fair flaxen colour, skin perfectly white all over the body, but of a curious thick texture. These genetic facts do not fit in with any genetic theory. There are difficulties in assuming either the father or the mother to have been heterozygous, and the presence of three white children and no blacks is unaccountable. They were not true albinos since they had brownish eyes, and if this represents a real germinal variation (mutation), then it would form an exact analogy to the way the white race may be supposed to have originated from coloured (not negro) ancestors. But without a more complete investigation of the case few conclusions can be founded on it.

* This term means brothers and sisters taken collectively.

Zimmermann (1923) describes five families with twelve typical total albinos, the condition being recognised as a Mendelian recessive. In three other pedigrees 31 of the members were albinoid, and in addition two sporadic cases of partial albinism are described. Pardo-Costello (1926) describes a family with 11 cases (6♂, 5♀) of congenital partial albinism in four generations. The condition consists of milky white patches on the skin, irregularly distributed and often symmetrically placed, the distribution being more or less the same in all members of the family. The individuals were otherwise normal. The inheritance is that of a Mendelian dominant, but the sibs of three generations number ten affected : five normal. This departure from equality may be due to chance, as the four children of the last generation are all affected, although having but one affected parent.

Three other (unpublished) cases of albinism may be given here. The C. family of Montreal consisted of three normal and four albinotic children. Their parents were normal and all the ancestors for two previous generations. This is apparently recessive albinism coming out, the only surprising feature being the ratio of 3 : 4 instead of 3 : 1. The G. family in London consists of five children, all albinos but the second sister, who is rather a brunette. They are also myopic, while the parents, who were first cousins, are normal and have excellent sight. No other cases are known in the ancestry, but fair complexion is common in this family in childhood. The L. family, of Southsea, is another albinotic case of white patches on the skin. The father had white patches on his body and neck. At seventeen, similar patches appeared on the daughter, and by the age of twenty had extended to the neck and face, so that the condition was more pronounced than in the father. A son and another daughter are normal. There was no albinism on the mother's side, although there were large families for three previous generations, but the father's mother's sister had the same marks, although the father's mother apparently had not.

Wlissidis (1928) describes a family with four albinos (all males) having white hair and eyelashes and pink eyes, and twenty-three blonds in five generations. The parents of the albinos (two families) were all dark, not blond. Blondness is inherited as a recessive to dark, except that in one family two blond parents had three blond and two dark children, and in another, a blond and an albino had one dark and three blond

children. The albinos were affected with nystagmus and were myopic. There may be a greater frequency of albinism in very fair families.

In an English family the inheritance of a white forelock has been traced through six generations by Harman (1909). The white forelock is accompanied by a patch of white skin spreading like a flare down the middle of the forehead. In some members of the family there are also patches of pure white skin on the median line of the trunk or the inner sides of the calves. The eyes were normal, with no white eyelashes or particoloured irides. The members of the family are long-lived and robust, but have a tendency to early whitening of the hair. This piebald marking was found in twenty-four individuals belonging to nine childships among a total of 138 individuals in the six generations. The children of normals were all normal. In the first three generations all showing the mark were females, but in the last three generations affected males and females were equal in numbers, and inheritance was thought to be through the males only. The data indicate, however, that the peculiarity is inherited as a simple Mendelian dominant, chance accounting for the absence of affected males in the early generations, and the small number of females who were mothers in the later generations accounting for the later lack of transmission through the mothers.

Pearson (1921) has since described another very similar case, with a white patch or flare on the forehead and hair. In this family there were seven affected members in four generations. This family also goes grey very early, and there is some tuberculosis but no consanguinity. This feature, of course, resembles the white " star " marking often seen in the forehead of horses and cattle, and frequently accompanied by white patches on the extremities. In this family the original great-grandmother in the pedigree must have been heterozygous. In the succeeding three generations the numbers of members which were normal or flared were respectively 3 : 2, 4 : 1, and 6 : 3, making a total of 13 : 6. This is a rather wide departure from the ratio which would be expected if the trait were a simple dominant, the odds against its occurrence being 17·5 to 1. But since unaffected members never transmit the flare, it cannot be a regular recessive. If the character is, as in other cases, a simple dominant, the small numbers showing the flare might, perhaps, be accounted for on the assumption of the decreased viability of such heterozygous individuals.

The occurrence and inheritance of a differently coloured, usually white, patch of hair, is a fairly common phenomenon. Darwin (*Animals and Plants under Domestication*, chapter xii.) cites an English family in which " for many generations some members had a single lock differently coloured from the rest of the hair," and an Irish family in which a small white lock occurred in son, mother, and grandmother.

Cockayne (1914) states that piebalds are very uncommon both in black and white races. He describes a piebald English family of six generations with nineteen affected members, belonging to a farming stock near Bury St. Edmunds, Suffolk. Some members of the family are fair and some dark, but both inherit the peculiarity, which consists of a blaze in the forehead. Three members of this family have heterochromidia iridis, and some have additional white patches of skin on the body.

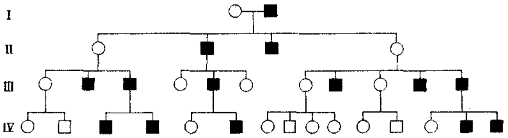


FIG. 35.—FAMILY SHOWING A WHITE FORELOCK.

In the last four generations of affected families the total numbers are seventeen having the flare to twelve* normal. This is near enough to the equality which would be expected if the flare were a heterozygous dominant condition, and is in general accord with Pearson's case; but the excess is on the other side and is, perhaps, not significant in either case. We may, then, conclude that the flare behaves as a simple domiuant, at least in these three independent families, and in the two described in the following paragraphs.

A family with a white forelock occurring in four generations has been described by Holmes and Schofield (1917). This lock occurs in the centre of the fore part of the scalp, the region affected being quite small (size of a florin). Heterozygous females do not show the mark. It would appear that the character behaves as a dominant in males and as a recessive in females (see Fig. 35), like the inheritance of horns in crosses of a breed of sheep in which only the males have horns with

* One of these is doubtful.

one in which both sexes are hornless. In a white forelock family, described by Pearson, Nettleship, and Usher in the monograph on albinism in man, the white lock occurred only in males, but was transmitted through females, skipping a generation in each case.

A much more interesting and extensive pedigree of a white lock family is given by Miller (1915). In this family the condition has been traced through six generations, including 203 individuals. Dr. W. B. Little, whose mother is known to have had the lock, emigrated from Carlisle, Englaud, to New Brunswick, Canada, about 1824, and his descendants through four generations show the white lock or flare. Some members of the family also have one or more colourless spots on their bodies. The condition behaves as a simple dominant, since in families with one normal and one marked parent the numbers were fifty-one normal and forty-five with the flare (where equality would be expected); and where both parents are normal all the children are the same. This family traces its origin back through the Percys and Mortimers to Edward III. That the white lock is, at least, as old as the family of Harry (Hotspur) Percy is known by the tradition that the white lock originated in connection with his death at the battle of Shrewsbury in 1403. When the news of his death reached his wife, she is said to have swooned and to have given birth shortly afterwards to a son bearing a white patch on his forehead. One member of the family has found from other records that the patch goes back at least to the Percys. It happens, also, that Lady Percy was an albino. The white flare may therefore, possibly, have originated with her, for although no such case is on record, it is known (see next paragraph) that spotted mulattoes arise from an ancestry in which different types of skin pigmentation have been involved.

Another interesting case, first recorded by Simpson and Castle (1913), is of spotting arising in a coloured race. It originated as a novelty—a spotted woman born from ordinary mulatto parents in Louisiana in 1853. No case of spotting had previously been known in that part of the country. She married a normal black negro, and their children numbered fifteen, eight spotted like the mother, and seven normal, but varying in depth of colour as is usual with mulattoes. Hence she was heterozygous. Three of the normal children and three spotted married normal negro mates. The normals had in all seven children, all normal. The spotted had in all nine spotted

and two normal. This indicates that all the spotted individuals, male and female, behaved as heterozygotes, and that complete segregation occurs between spotting and non-spotting. The fact that spotting appears rarely and sporadically among the innumerable mulatto crosses tells strongly against it being the result of an inherited spotting factor. The particularly clear evidence here indicates that it arises as a mutation in the hybrid stock, the original spotted individual being heterozygous and the piebald condition dominant to normal mulatto pigmentation.

Much interest was taken in such pied or spotted individuals in earlier centuries, and some famous ones were brought to Europe and painted. An early record of such pied individuals is found in a paper by J. Morgan (1786) in Philadelphia. A girl two years of age born in St. Lucia, West Indies, had a clear black skin verging to brown, except for a white spot an inch wide on the forehead, extending from the root of the nose upwards into the hair, which was also white on this area but curly like that of a negro. There was a large black spot in the middle of the forehead. The inner half of each eyelid was white and there was a white spot on the chin. The upper and middle arms were white with black spots; the breast, abdomen, arms, and thighs were mostly white. This is fairly typical of the classical piebald marking.

Another case, probably of a different kind, is cited of a boy two years old born in Guadeloupe from a negress and a white man. The father had spots of deeper white on his body and the son showed the same distribution of spots. The father's mother and one brother had the same markings. This appears to be a case of inheritance of a spotting pattern in a white family.

With regard to the ancestral colour of man, it seems clear that the most primitive races were black (as John Hunter concluded 150 years ago), or at any rate dark, as they are now, and that the white race arose from them with loss of pigmentation. It appears unlikely that a simple mutation was involved. Although albino mutations occur in black races, the "white" man's skin is by no means devoid of pigmentation. It appears probable that many small germinal changes affecting pigmentation were involved. The known relations between skin pigmentation and the adrenal capsules indicate that germinal changes which affected the activity of these glands were really involved. From recent studies of the endocrine gland secretions, it appears that differences in the activities of various endocrine

glands are responsible not only for the differences in pigmentation of the various races of mankind, but also for their characteristic physiognomies.

In the same way, it is highly probable that brown was the primitive eye colour in man, and that blue arose from it through one or more mutations, with loss of pigment. It may be that blue arose originally as a simple mutation from brown, and that intermediate shades have come in later. This has been shown to be the history of various cases of melanism in *Lepidoptera*. But at present there is no definite evidence to prove the point either way as regards man. When blue eyes were once established, they multiplied in the northern races, perhaps through sexual selection, until blue eyes are characteristic of the Scandinavian and other northern peoples. But the native peoples in tropical countries appear always to have retained brown eyes, the pigment probably being a protection for the eye against the strong rays of the sun. The white race is thus in a sense an albinotic variation, which has arisen through loss of pigmentation. This loss has been carried still further in the more northern races with fair complexion, light hair, and blue eyes.

In the Pearson monograph on albinism many early records of albinotics are considered. It is concluded that there is no evidence that a tribe or clan of albinotics ever existed, but there are numerous records indicating the existence of considerable numbers of albino individuals. In connection with Dampier's expedition to Darien in 1681, there is a long and circumstantial account of the "white Indians," who could see better by moonlight, etc. There is a similar record for Brazil in 1775. Cortez, in connection with the Spanish conquest of Mexico, described Montezuma's palace as containing an entourage of albinos. In a similar way, in the Middle Ages, fools and dwarfs were considered a desirable accessory to the retinue of kings and nobles. As late as 1841 Catlin (1926) described a "white Indian tribe" in Upper Missouri containing many albinos. It appears that albinism is now most frequent among the Indians of Arizona and Mexico. Poole, in 1872, reported light-haired and fair Indians from Queen Charlotte Islands and British Columbia.

But the most striking case of albinism on record is that of the so-called white Indians of the San Blas coast and Darien. The earliest full account of them is by Wafer (1699), and the fullest recent description is by R. G. Harris (1926). Shrubsall

Haddon, and Buxton (1924) also published notes on their observations of several individuals. They are a "race" of partial albinos, originating through mutation and perpetuated by inheritance, their peculiarities being recessive to the type. Their skin is white, with freckle-like copper-coloured spots. The hair may be yellow or may even show traces of brown. The iris is hazel, dark blue, or dark violet. They are strongly photophobic, and so are at a great disadvantage by day in strong sunlight, and they are generally smaller than the type. In 1924 several were brought to the United States and Canada, where they were studied by anthropologists. Although marriages between albinos are prohibited by the tribe, and white women rarely marry brown men, yet they have persisted in numbers for at least three centuries. It is instructive to know that a recessive condition can persist and spread in a population in this way even although it is under serious natural disadvantages and is further prevented from increase by tribal law.

There are said to be over 300 such white Indians. The usual proportion of albinism is about 1 in 10,000. In a population of 20,100 Indians, 138 albinos were found, a frequency of 0·7 per cent., or 50 to 100 times the usual frequency. Of 309 offspring examined from the matings of heterozygous brown individuals, 77 were white, 155 light brown or very light brown, and 77 brown. This is a perfect 1 : 2 : 1 ratio, and indicates clearly that a single recessive gene mutation was involved in the origin of the type. There is every reason to suppose that the peculiar types among the Mandan Indians in North America or the Nordic type in Europe originated and spread in similar fashion. We are thus furnished with an example of a racial colour type of man in the making.

Albinism is known in most races and probably occurs in all. Its frequency is unknown, but has been estimated at 1 in 5,000 or 1 in 30,000. In Germany, out of nearly four million children dealt with, about 400 had "white hair." This would give a frequency of 1 in 10,000. A similar proportion was found in Norway. Of the 400 only 32 had "red eyes," and of these only 23 had also white hair: hence only one complete albino in 200,000, but the true prevalence may be greater. In Austria, from statistics of insane albinotics, it was estimated that 1 in 400, or 1 in 2,000, of the population were albinotics. This very high estimate is probably due to correlation between albinism and mental derangement.

In Scotland 100 to 150 living albinos were recorded from

about half the population. This indicates a frequency of 1 in every 15,000 to 25,000 inhabitants. Moreover, less satisfactory records are available from many other countries and races. It appears that albinism occurs as a mutation in the absence of crossing of races, both in the dark and white races, but it also frequently arises, as we have seen, a generation or two after a mixture of races has taken place. The piebald, apparently arising only from cross-breeds, is far rarer than the complete albino.

Pearson also considers the pathological condition known as leucoderma (white patches on the skin), and finds there is no physiological differentiation from albinism, the two being distinguishable only by the inheritance of the latter. Pearson distinguishes between spotlings and piebalds, the former

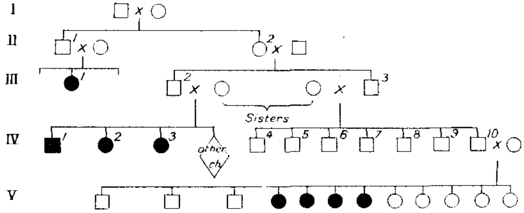


FIG. 36.—PEDIGREE OF ALBINISM IN A FAMILY.

including those with white markings which do not extend to extensive areas on the trunk. The extent of the leucosis is probably hereditary, but there is no sharp line between spotlings and piebalds. The spotling of one generation may be the father of a piebald in the next. Albinism, piebaldism, and leucoderma are probably all to be accounted for by the same metabolic defect. Leucoderma, however, is not necessarily inherited.

A family in which albinism was carried as a recessive for five generations is described by Sedgwick (1861). The pedigree of this family is given in Fig. 36. One of the original ancestors of generation I. must have been carrying albinism as a recessive. The wife of II. 1 must have been in the same condition. Their daughter, Josephine (III. 1), was the only descendant of this son to show albinism. The two grandsons, III. 2 and III. 3, married sisters, both of whom apparently carried albinism recessive. No. III. 3 had seven normal sons, five of whom

married, but only one of them had albino children. This family numbered three normal sons, and nine daughters, four of whom were albinos. The mother again must have carried albinism as well as the father, if the condition is, as usual, a strict recessive.

In another record of Sedgwick, two grandsons in a Swiss village had each two daughters, one normal and one albino. The albino great-granddaughters married. One had no children, the other had an imperfect albino by a husband with black hair and brown eyes. There was probably intermarriage in both these lines of descent.

Meirowsky and Spickernagel (1926) describe an albinotic family in which the same pattern of white patches on skin and hair could be traced through five generations and appeared as birth-marks. The inheritance was that of a dominant character.

Little (1920) mentions that a piebald coat characterises such breeds of dogs as foxhounds, beagles, Boston terriers, St. Bernards, and collies. The spotting reaches an extreme in bull terriers where normally only the eyes are pigmented. The origin of spotted individuals from typical ancestors is recorded in two pure breeds of pedigree dogs, and it is considered that they may have arisen through mutations. In the first a spotted female was born from two solid-coloured pedigreed and registered Scottish terriers, but since a certain dog occurs in both the male and female ancestral lines the outcrop of spotting would be accounted for if that animal were carrying a recessive factor for spotting. In the other case, four spotted puppies occurred in two litters of pedigree Airedale terriers. The pedigree of the five previous generations shows that one male occurred seven times and one female three times in this pedigree, the former occurring on both sides of each ancestral line. He was probably carrying a recessive factor for spotting, or possibly a mutation giving rise to this factor took place in his gametes.

The writer (Gates, 1909*a*) found in a cross between a pure-bred Old English sheep dog and a Scotch collie that F_1 dogs were produced with several different lengths of tail, or no tail, like the mother, and with many other differences in coat, build, and temperament. It is probable that almost all our pedigree breeds of domestic animals carry some recessive characters, never eliminated since the original crosses, which in many cases were the foundation of the breed. But these germinal

differences must have arisen at some time through germinal changes which gave rise to the parental types, although similar germinal changes may equally well occur afterwards and be carried as recessives in the germ plasm until a cross or inbreeding brings them out.

The Pearson monograph includes also a study of peculiarities of vision, such as night-blindness, as well as the hair, of albinotics, and also albinism in various animals. Complete albinos with pink eyes are known to occur in " pure " races of man, just as they occur in many mammals,* birds, and plants (white petals). The monograph above mentioned also includes a study of seasonal variation in animals that are white in winter, such as *Lepus variabilis* in Scotland. Crosses of white and black Pekinese dogs are also believed to furnish evidence of the *de novo* origin of spotting and blends. It is well known, of course, that in certain breeds, as the Dalmatian, particular types of spotting have become a fixed characteristic of the breed. Numerous Mendelian studies of spotting in mammals have been made in recent years, especially in rabbits, rats, and mice, and complicated theories of inheritance of spotting have been formulated. It seems clear that in many cases degrees of spotting and their inheritance can be explained on the basis of a series of factors for spotting. The evidence clearly indicates, I think, the sporadic *de novo* origin of spotting in man through crossing (see p. 112), but it does not follow that the same is necessarily true for dogs. In some breeds spotting, however attained, has the status of a germinal factor, and the regularity with which white-black crosses of Pekinese yield definite patterns would seem to indicate another mode of heredity behaviour—*i.e.*, that a spotting or pattern factor is present in these crosses.

Detlefson (1920) has described a herd of albino cattle on a farm in Minnesota with several points of interest. This herd originated from two albino calves—a bull and a heifer—which resulted from mating a " full-blooded " Holstein bull with " grade " Holstein cows. The parents had the normal black-and-white spotted coat colour, while the calves were pure

* There are records, for example, of albino beavers, chipmunks (*Tamias*), squirrels, woodchucks (*Arctomys*), robins (*Turdus migratorius*) and sparrows. Dean (1903) says: " True albinos occur among hag-fishes, and partial albinos are not rare." Standley (1921) refers to an early American record of an albino black bear with " four cubs, one white, with red eyes and red nails, like herself," showing that albinism must have been carried as a recessive in the strain.

white with pink eyes. The original bull produced these two albinos out of matings with about twenty grade Holstein cows, the remaining calves being normal. Unfortunately the original records of the herd were destroyed by fire, for the later breeding behaviour of these two albinos is peculiar. From its manner of origin one would expect the albinism to be present as a recessive character in the germ plasm of this herd. But the young albino bull mated to grade Holstein cows produced only albino offspring—about twenty in number. The albinos mated *inter se*, moreover, produced only albinos, and four albino cows mated to a registered Holstein bull (the original bull had been killed) produced three albinos and one normal. It is not certain from these later matings that the albinism behaved as a simple dominant, for there is no record of coloured offspring from two albino parents. But, at any rate, the later hereditary behaviour is different from that at the time of its original appearance as a mutation, and it is not clear that this change in behaviour can be explained merely as a reversal of dominance.

The albinos showed no pigment in the skin, eyes, horns, or hoofs, except in one cow which had a small black spot about one centimetre square in one ear. There was no alteration in milk-production, but the albinos were extremely sensitive to light, and grazed listlessly during the day with partly closed eyes. Such albinos are, of course, quite different from the famous Chillingham and Chartley herds and other races of white cattle. The evidence indicates that in these the white is a dominant, and that they are descended from original prehistoric wild white cattle in Britain (see Storer, 1881, and MacDonald and Sinclair, 1882). They are not pure white, but had typically black hoofs and muzzle, a circle round the eyes, black tips to the horns, and in some cases a black tip to the tail. Wild white cattle from Thessaly, etc., were also known to the Greeks and Romans, and in Italy a white breed, in which the calves are yellowish, continues down to the present time.

Hadwen (1926) points out the disabilities that white varieties of wild and domesticated animals suffer. The white reindeer, of which the Laplanders keep a few to make it easier to follow the herd in summer, are deficient in many respects. They are not true albinos, having bluish-grey eyes, but they sleep much, their eyes are weak, their sense of smell deficient, and they are easily a prey to wild animals. The normal reindeer has a

lighter (yellow, brown, grey, or white) coat in winter, but sheds this for a dark one in summer which is a defence against the sun. The white reindeer suffer through remaining white all summer. Flies also attack light animals more than dark. Similarly, Holstein Friesian cattle suffer from sunburn or scald only on the white portions of their hide, and white pigs may lose the skin from their entire backs through sunburn. The genetics of the white reindeer have not been investigated.

Three types of albino horses have been described (Wriedt, 1918) in two Norwegian breeds. The heterozygous condition is intermediate in these horses, and albinism appears to behave nearly the same as in guinea-pigs.

Civilisation has often been credited with the production of the numerous congenital deformities that appear in man. But various studies, such as that of Stannus (1914) on the Bantus of Nyasaland, show that the same abnormalities continue to appear, probably with equal frequency, in native races, even though the more marked of them are ruthlessly eliminated by infanticide. It is evident that the conditions of civilisation tend rather to preserve than to originate abnormalities, and that natural selection in native races, as in wild animals, combined with parental selection, tends to eliminate individuals possessing characters which place them at a disadvantage in the struggle for existence.

LITERATURE

Catlin, G. 1926. North American Indians. Edinburgh: John Grant, 2 vols.

Cockayne, E. A. 1914. A piebald family. *Biometrika*, x. 197-200, pls. 9.

Davenport, C. B. 1916. Heredity of Albinism. *Journ. Hered.*, vii. 221-223.

Detlefson, J. A. 1920. A herd of albino cattle. *Journ. Hered.*, xi. 378-379, figs. 2.

Gates, R. R. 1909. A litter of hybrid dogs. *Science*, xix. 744-747.

Gates, R. R. 1915. The modification of characters by crossing. *Amer. Nat.*, xlix. 562-569.

Hadwen, S. 1926. Colour in relation to health of wild and domestic animals. *Journ. Hered.*, xvii. 450-462, figs. 9.

Harman, N. 1909. A study in heredity. Six generations of piebalds. *Trans. Ophthal. Soc.*, xxix. 25-33.

Harris, R. G. 1926. The San Blas Indians. *Amer. Journ. Phys. Anthrop.*, ix. 17-63, figs. 5.

Holmes, S. J., and Schofield, R. O. 1917. Inheritance of white forelock. *Journ. Hered.*, viii. 359-360, fig. 1.

Little, C. C. 1920. A note on the origin of piebald spotting in dogs *Journ. Hered.*, xi. 12-15, figs. 3.

MacDonald, J., and Sinclair, J. 1882. History of polled Aberdeen or Angus cattle. Edinburgh and London: Blackwood, pp. 459, illustr.

Meirowsky, E., and Spickernagel. 1926. Über Vererbung und Lokalisation der Scheckenbildung sowie ihre Bedeutung für die Nævusätiologie. *Arch. f. Dermat. u. Syphilis*, cl. 384-392, figs. 9.

Miller, Newton. 1915. Heredity of white forelock. *Journ. Hered.* vi. 165-169, figs. 4.

Morgan, J. 1786. Some account of a motley coloured or pye negro girl and mulatto boy, exhibited before the Society in the month of May, 1784. *Trans. Amer. Phil. Soc.*, ii. 392-395.

Pardo-Castello, V. 1926. Congenital partial albinism. *Arch. o Dermat. and Syph.*, xiv. 173-177, figs. 3.

Pearson, K. 1913. Note on the Honduras Piebald. *Biometrika*, ix. 330-331, pls. 4.

Pearson, K. 1921. A new white-lock family (Barton's case). *Biometrika*, xiii. 347-349, pls. 2.

Pearson, K., Nettleship and Usher. 1913. A monograph on albinism in man. Drapers Company Research Memoirs, Cambridge Univ. Press, in 4 parts.

Sedgwick, W. 1861. On sexual limitation in hereditary disease. *Brit. and Foreign Med.-Chirurg. Review*, xxvii. 477-498, xxviii. 198-214.

Shrubsall, F. C., Haddon, A. C., and Buxton, Dudley, L. H. 1924. The "White Indians" of Panama. *Man*, xxiv. 162-164, figs. 4.

Simpson, Q. I., and Castle, W. E. 1913. A family of spotted negroes. *Amer. Nat.*, lxvii. 50-56, figs. 4.

Standley, Paul C. 1921. Albinism in the black bear. *Science*, liv. 74.

Stannus, H. S. 1913. Anomalies of pigmentation among natives of Nyasaland. *Biometrika*, ix. 333-365, pls. 10.

Stannus, H. S. 1914. Congenital anomalies in a native African race. *Biometrika*, x. 1-24, pls. 6.

Stiven, H. E. S. 1923. A Sudanese albino. *Lancet*, cciv. 648, fig. 1.

Storer, Rev. John. 1881. The wild white cattle of Great Britain (New Edition). London: pp. 384, figs. 12.

Wafer, Lionel. 1903. (Rep. from original edition of 1699). A new voyage and description of the Isthmus of America. Cleveland: Burrows Bros. Co.

Wlissidis, Thr. 1928. Über einen Fall von allgemeinem Albinismus mit Nystagmus. *Verh. V. Internat. Kongr. Vererb.*, ii. 1601-1602, fig. 1.

Wriedt, Chr. 1918. Albinisme i hester. Borket, hvitborket og gule. *Tidsskr. Norske Landbr.*, 396-406.

Zimmermann, H. 1923. Über menschliches Albinismus. *Arch. f. Rassen. u. Gesells.-Biol.*, xv. 113-136, figs. 8.

CHAPTER VII

VARIOUS SKIN CHARACTERS AND SKIN DISEASES

SKIN colour and certain other characters of the skin are considered in connection with racial crossing (p. 313). Here variations of other kinds, and abnormalities, may be considered. Numerous pedigrees of ICHTHYOSIS exist. A celebrated case often referred to in the early literature is that of the "porcupine man," Edward Lambert. The first account appears to be that of Machin (1733). A country labourer exhibited his son, who was then fourteen, in London. The son had a very scaly skin which did not bleed when cut, but was callous and insensible. The skin was said to be shed every year in the autumn, a new skin growing up underneath. It had "bristly parts" about the belly and flanks, which rustled like the quills of a hedgehog. He was born normal, but the skin began to turn yellow at the age of seven or eight weeks, then by degrees changed to black, then thickened and grew into its present condition. The parents were apparently normal and had "many other children," none of which showed this deformity, which seems to have been an extreme form of keratosis.

Further details of this individual are given (Baker, 1755) when he was about forty years old. The skin most nearly resembled "an innumerable company of warts," of a dark brown colour and near an inch in height when fully developed. His head and face, palms and soles, alone were free from this condition. He now had six children, all with the "same rugged covering as himself," the condition making its first appearance about nine weeks after birth. The describer draws some interesting conclusions which we may quote in his own words: "It appears, therefore, past all doubt, that a race of people may be propagated by this man having such rugged coats or coverings as himself; and if this should ever happen, and the accidental origin be forgotten, 'tis not improbable they might be deemed a different species of mankind: a consideration which would almost lead one to imagine that if mankind were all produced from one and the same stock, the

black skins of the negroes, and many other differences of the kind, might possibly have been originally owing to some such accidental cause." In modern language we should call this individual a simple dominant mutation, like so many of the other abnormalities in man.

According to Sedgwick (1861), this condition was perpetuated for two more generations, two brothers of the fourth generation visiting Germany in 1802. They had seven sisters who were normal, from which it would appear that the character was *male-sex-linked—in other words, recessive or suppressed* in the presence of the normal X chromosome in females, and dominant or finding expression in the presence of the Y chromosome in males.

A less extreme form of the same condition (Martin, 1818) was Jane Holden, aged three, whose whole skin except the face was " covered with small scales, or rather warty or bristle-like projections," light brown to black in colour and constantly exfoliated. The condition began at the age of three months. Her mother was the same, except that the neck, breast, and forearms, as well as the soles of the feet, were free from this condition. Her parents were healthy, and she was the only one of six children having the disease. In this family, unlike the previous ones, the condition is therefore not male-sex-linked.

That ichthyosis congenita is lethal (abortions or premature births or dying after two or three days) in the homozygous condition is indicated by a case cited by Mohr (1926). A normal woman had five normal children by a normal husband, then three congenitally ichthyotic children by her half-brother.

Still less severe forms of ichthyosis were formerly said to be rather frequent on the Continent, and were called " pellagra." Sedgwick (1861) quotes Italian statistics among the peasants of Lombardy, in which, in 184 families, there were 671 healthy individuals and 648 showing pellagra. From this it would appear that the condition perhaps involved a simple Mendelian recessive character. In modern studies of pellagra (see Davenport, 1916) in Italy, the United States, and elsewhere the essential symptoms appear to be inflammation and ulcerations of certain areas (often symmetrically placed) of the skin, often accompanied by diarrhœa from ulcerations of the intestine. These symptoms are due to the presence of a toxic agent, which may also induce nervous and mental disturbances in some individuals. Variations in these symptoms are partly due to

differences in the hereditary constitution of affected individuals, leading to differences in the susceptibility or resistance of various organs to the toxin. Davenport considers that pellagra is probably communicable, but the history of the disease will depend entirely upon the constitutional conditions of resistance which it meets in the organs of the body. When both parents are susceptible to the disease, nearly half the children are susceptible, while the disease affects less than 1 per cent. of the whole population (statistics from Spartanburg Co., South Carolina). The high incidence in certain strains will, then, be due partly to infection, but also depends on susceptibility, for susceptible and non-susceptible children often occur in the same family. Pellagra thus bears certain resemblances, from an inheritance point of view, to tuberculosis, cancer, and leprosy. A more recent pedigree of male-sex-linked inheritance of ichthyosis is compiled (Fig. 37) from data given by

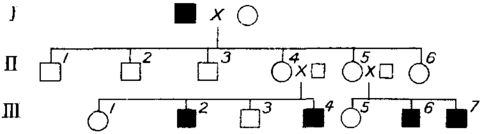


Fig. 37.—Pedigree of Male-Sex-Linked Ichthyosis. (From Sedgwick)

Sedgwick (1861). The condition is evidently transmitted by females to half their sons.

Orban-Vadja (1925) records a similar case of the disease, transmitted by females and appearing in males. Pick (1925) notes a case of two brothers affected, six other children healthy, the parents unrelated.

In another family, cited from Cunier, thirteen cases of ichthyosis are recorded in five generations, and all the affected individuals were females. The condition was therefore female-sex-linked in this family. The character must then behave as a dominant in the females of the latter family and as a recessive in the females of Sedgwick's family. All pedigrees except Cunier's appear to follow the rule for male-sex-linked inheritance. Lundborg (1926) describes a Swedish peasant family in which ichthyosis is transmitted by the females in four generations, but found only in the males. An apparently milder form of the disease, with a rough dry skin, is shown,

however, by the pedigree of Manson (1928) to be a simple dominant, occurring in both sexes in three generations. Wehefritz (1924) also gives a pedigree of inheritance as a dominant, but in which a generation may be skipped.

KERATOSIS is a closely related condition, occurring also in different degrees and forms. Gossage (1908) gives a pedigree showing keratosis or abnormal thickening of the skin of the palms and soles. It is a non-sex-linked dominant, occurring in both sexes. He cites from the literature 28 families with a total of 222 affected and 184 normal sibs. In 19 of the families there is an excess of affected. Siemens (1925) describes the inheritance of two forms of keratosis. A pedigree of K. follicularis shows twelve cases in four generations of a family in Utrecht. The inheritance was of the ordinary male-sex-linked type and was accompanied by degeneration of the cornea and progressive loss of hair (alopecia). In the other pedigree, of a family in Munich (four generations), the condition shows partly in both males and females, but without the corneal degeneration. Men exhibit the changes both of skin and hair, while women carriers have keratosis without loss of hair. The daughters of affected men and the sons of affected women both have it, but sons of affected men are free. Hence it follows the X chromosome in inheritance, but the dominance is incomplete, and in women irregular.

Various hereditary forms of EPIDERMOLYSIS BULLOSA are known—a condition of the skin in which slight friction or abrasion causes the formation of large blisters. It is usually dominant, but one form is recessive. Jenny (1927) describes a very severe form which is fatal a few weeks or months after birth, and may therefore be regarded as due to a lethal gene. The pedigree was traced back into the eighteenth century. Two families were investigated, and in each case the parents of those affected were shown to be remotely related. Evidently in this case a recessive lethal defect was passed down through six or seven generations before a mating of two individuals heterozygous for the condition brought it out.

The view has been held that the dystrophic form of the disease is recessive, and the simplex form dominant. Against this, Hofmann (1926) produces a pedigree of the dystrophic form showing dominance. From several pedigrees he concludes that the severe form is recessive and the mild form dominant.

Hope and French (1908) describe a family in which per-

sistent hereditary *œdema* (swelling due to the effusion of watery liquid into the connective tissue) is traced through five generations, appearing in thirteen out of forty-two individuals. This was accompanied by nervous attacks in many cases. The inheritance, as shown by the pedigree, is in accord with that of a Mendelian dominant, except that one normal female has an abnormal child in a family of six. The swelling of the legs, which was extreme in certain cases, was usually kept down by wearing bandages. Several individuals lived to over seventy with their legs bandaged, having had the malady for sixty years or more. This condition was first described by Milroy in America, where it was traced through six generations, and similar cases of hereditary œdema have been described in France and England. Bulloch (1909) gives nine pedigrees of trophœdema (with permanent swelling of feet and legs), and finds it rather more common in females than in males. In a total of seventy-three affected individuals observed, forty-one were of the former sex and thirty-two of the latter. Bulloch (1909) also describes angioneurotic œdema,* or acute circumscribed œdema, in which there are local swellings of the limbs, trunk, and face, and the mucous membrane may also be involved. The swellings are temporary, but often show remarkable periodicity. There is direct inheritance in a number of instances, or the disease may occur as a family complaint.

Epiloia is a rare condition in which the symptoms are partly cutaneous and partly nervous (Brushfield and Wyatt, 1926). Adenoma sebaceum, involving a deficiency of the sebaceous glands, appears at the sides of the nose in the fourth or fifth year. It may be accompanied by mental deficiency or idiocy, epileptic fits, and cerebral abnormality. The condition is apparently confined to Europeans and is found among the poorer classes in Great Britain. It is said to be commoner among girls than boys. Sixteen cases were studied in the Fountain Mental Hospital in twelve years. The data of heredity are too scanty to determine the method of inheritance, but either the mental or the cutaneous symptoms were found in some of the relatives.

Hadley (1927) describes an epithelial defect in calves, which he calls *epitheliogenesis imperfecta neonatorum bovis*. A calf showing

* This is a condition in which there is swelling in patches by the accumulation of blood in the connective tissue, owing to a disorder of the vasomotor system affecting the bloodvessels.

it was born in the pure-bred Holstein herd at the University of Wisconsin. The skin below the knees and hocks was defective, the feet had one or more undeveloped claws, the ears were deformed, and there were defects in the integument of the muzzle and in the mucous membrane of the nostrils, tongue, hard palate, and cheeks. The calf soon died from septicemia through infection. Fifty such calves have appeared in fifteen Holstein herds in several generations. The lesions were practically identical in every case, and lethal in effect. This condition is evidently due to a recessive lethal gene mutation, brought to light by inbreeding.

Siemens (1926) investigated the inheritance of ACNE, a chronic disease of the sebaceous glands, in which the skin, especially of the face, breaks out in pimples, particularly at puberty. Erasmus Darwin referred to its inheritance in 1797 and distinguished it from similar conditions. From a study of acne, rosacea, and related conditions in monozygotic and dizygotic twins, Siemens found that in 36 pairs of monozygotic (identical) twins they showed great similarity and only slight differences as regards these diseases. But 12 pairs of dizygotic twins nearly always showed strong differences. Siemens suggests a polyhybrid inheritance for acne, due to several independent factors. It is regarded as essentially an allergic disease (*q.v.*).

In a child with XERODERMA PIGMENTOSUM the skin becomes inflamed when exposed to the sun, forming red spots from which cancer may develop, usually leading to death before maturity. Usually it begins in the first three years, and two-thirds of the cases die before the fifteenth year. In a study of its inheritance, Siemens and Kohn (1925) have collected 333 cases in 222 families. Of these, 187 were familial (in 76 families), the rest solitary. There is no sex-linkage, as the condition is found in 149 ♂ : 152 ♀. The children of persons with xeroderma pigmentosum are said to be always free from it. It is not associated with other malformations or diseases. Generally it appears as a simple recessive, but there are some exceptions, due either to the failure of some homozygotes to show it (*i.e.*, it is an irregular recessive), or there may be cases of xeroderma which have a different ætiology. Mohr (1926) finds evidence that the condition is lethal in effect when homozygous.

XANTHOMA (cholesterosis cutis) is described by Fasold (1924) in 15 families, with 58 normal : 53 affected sibs. It is inherited, at least for the most part, as a dominant, but the dominance

is very irregular and frequently a generation (or in one case two generations) is skipped.

Wiener (1925) describes the inheritance of the condition known as CUTIS LAXA, or rubber skin, in which the whole skin is movable and extensible. It could be pulled up 7 or 8 cm. on the breast of a man, and the patient was not inconvenienced except that large and painful hæmatomata appeared under the skin after an accident or when stretched too far. The pedigree shows 10 cases in three generations, the inheritance a simple dominant.

PSORIASIS is one of the most common skin diseases, in which unhealable sores appear on the arms and legs. The conditions vary much and the inflammatory marks may fail to appear for long periods. Heiner (1926) describes four pedigrees of this condition, in which it appears as a dominant which not infrequently skips a generation. One family shows 10 cases in four generations. In all sibships there were 34 affected: 29 normal, but 63 per cent. of the afflicted were males and only 37 per cent. females.

Meirowsky and Leven (1921) have made a study of various skiu markings and BIRTH-MARKS in mau. Meirowsky and Bruck (1921) give a pedigree showing the inheritance of a birth-mark, in which seven individuals out of eleven in three generations had the mark. It was inherited as a direct dominant through both sexes.

Leven (1927) describes a single case in which dappled white spots on the skin occurred with spotting of the teeth. The former was a form of albinism, as shown by the failure of the patches to develop pigment when exposed to ultra-violet light. Other cases of tooth-spotting have been described by Bampton, in which the condition is dominant. Nothing is known of the inheritance of the dappled spots, and it is probably only by chance associated with spotted teeth.

HAIR.

The colour and shape of human hair have been referred to elsewhere (p. 313), and here the inheritance of differences in quantity of hair may be considered. In a study of the inheritance of BALDNESS, by Dorothy Osborn (1916), she tabulated the results for twenty-two families and reached some definite conclusions. Baldness is found to be a sex-limited trait, being inherited as a dominant character from father to son. In a

woman it acts as a recessive, and may be transmitted as such, only appearing as baldness when present in the duplex (homozygous) condition. This would explain the greater rarity of baldness in women. Baldness is frequently associated with progressive decrease in the concentration of thyroid in the blood, and it is said that eunuchs do not become bald. The view of early baldness as a sex-limited trait is borne out by data of Sedgwick (1863).

Baldness is no doubt commoner in some races than in others. Jenness (1928, p. 104) observed a single Eskimo in the Coronation Gulf region who was bald. He had a seventeen-year-old son nearly as bald as his father. There were no infectious diseases, and the condition must have been inherited. Fantham (1925) observed a South African family of English descent with a small bald spot about an inch across over the left ear. There were ten cases in three generations. It occurred in both sexes and behaved as a simple dominant, except that in one case it skipped a generation.

Fantham (1924) describes a Transvaal family with early baldness, all the men (nine in three generations) becoming prematurely bald with the same "skull-cap" pattern, while the women have abundant hair. In the grandfather the onset of baldness was at twenty-one, in all the others at about eighteen, with rapid loss of hair above the level of the ears. In this family the inheritance is entirely through the males to their sons, and there is no evidence as to whether women can transmit the condition. If it is confined entirely to the male line it would be another case of presumed transmission in the Y chromosome. Fantham also describes a family with rings of white hair at the nape of the neck and near the right-hand parting, nine cases in four generations. As in the last pedigree, it is found only in the men and is transmitted from father to son, but skips a generation in one case, a normal father having three sons with it. The evidence again is insufficient to be certain that women do not transmit, but one woman who might be a carrier has two normal sons.

Duerden (1918, 1919) has shown that in crosses between the North African and South African ostrich the bald spot of the former behaves as a simple dominant character, not sex-linked. In the chicks the head is covered with a bristly down, but in the North African birds this gradually falls out during the first few months and is not replaced by feathers.

Premature whitening of the hair is undoubtedly inherited,

but the data for a pedigree have not been collected in many cases. Hare (1929) describes a family with nine cases in five generations. The inheritance was that of a simple dominant, as it occurred equally in both sexes. Beginning at seventeen or eighteen, the hair turns slowly white, becoming completely so at twenty-five or twenty-six. In two cases, by careful treatment of the hair (without dyeing) the colour was retained.

Another inherited variation pertains to the occipital hair whorl. Bernstein (1925) finds that a clockwise direction of the whorl is dominant over anticlockwise. Lauterbach and Knight (1927) also discuss variations in the whorl, which in some cases is double. Schwartzburg (1927) finds by examining schoolboys that the head whorl is four times as frequently an anticlockwise (+), or left-handed spiral, as clockwise (−), or right-handed, the latter dominant in accordance with Bernstein, the two making a simple Mendelian pair. The double head whorl occurred in about 7 per cent. of cases, and double whorl was a simple recessive to single whorl. Among double whorls − − and + + are very rare, and − + is much more frequent than + −. Among 3,400 boys, only 21 had double whorls which were − − or + +. Of the 4,259 boys examined, 18·6 per cent. were +, 74·4 per cent −, and 7 per cent. double.

Many studies relate to the quantity of hair on particular parts of the body. Hypertrichosis and hypotrichosis may both be inherited, as well as alopecia (complete loss of hair). Races also differ in the hairiness of their bodies, the negro having least hair; the white races have a considerable quantity, and the Ainu perhaps most. Many degrees of hairiness of the body exist, and are probably inherited as units. *Hypotrichosis congenita familiaris*, in which the children are born hairless or the hair disappears in the first few months of life, is recorded by Gossage (1908) in 7 families as dominant to normal, with 26 affected members. "Dog-men" or "ape-men," with hair covering the face, including the nose and upper eyelids, are rare, and according to Danforth (1925) probably not more than 30 different families are known, including famous ones from Russia and Burma, but the condition is inherited as a dominant and is characteristically accompanied by deficient dentition. Von Luschan estimates that a new case occurs about once in a thousand million of population. Danforth (1925) summarises a great deal of other knowledge on the inheritance of hair conditions.

Trotter and Danforth (1922) made a study of *facial hyper-*

trichosis in women. It has generally been regarded as a result of endocrine disturbance, but there is little evidence for this, and it appears to be due to germinal factors controlling the amount of hair. Out of 350 women college students, 94 had facial hypertrichosis (or 26·8 per cent.). It was found that coloured women and insane women showed about the same frequency of hypertrichosis, and it is not associated with reduced fertility. As regards inheritance, since the condition cannot be recognised in the male, its statistical frequency in the female was calculated on the assumption of a dominant factor being concerned, and this gave results in accordance with the observed frequency. Danforth (1921) has also made an investigation of the distribution of *hair on the digits* of man. Complete absence of hairs from the middle segments of the digits is a recessive trait. It is a useless character, yet widespread. The tendency to lose the hair from the terminal and middle segments of the digits is present both in man and the anthropoids. Man alone has lost all hair from the terminal segments. The inheritance was studied in 80 families with 178 children. With the exception of five children in two families, no child exceeded the degree of digital pilosity of the more hairy parent. The progressive phylogenetic loss of hair from the digits appears from these observations to be brought about by one or more recessive genes, or a main gene with modifying factors, of which sex may be one.

A family with hypotrichosis was described by Berglund (1925). The third child in a family of ten had hypotrichosis, being congenitally devoid of head hair. He married two normal wives, and five of their ten children were normal, indicating a simple dominant. Gossage (1908) records it in seven families, apparently dominant.

ALOPECIA may be produced by disease, but it also occurs as an inherited condition. Danforth cites a pedigree from Linzenmeier with 19 cases in five generations, the inheritance being dominant. But it also appears from normal parents, indicating a recessive condition, and it may be sex-linked in certain pedigrees.

In a little-known work on the hair of mankind, Friedenthal (1908) gives descriptions with numerous coloured plates showing the distribution of hair on the human body, and the extremes of plus and minus variation in various races of man and some apes. Ainu of Japan are figured, in some of which almost the entire body has a hairy covering, and these are compared

with certain European variations in which the whole face is covered with hair. Darwin* cites a Siamese family which for three generations had the face and body covered with long hair. This was accompanied by deficient teeth. He also refers to a woman with completely hairy face, exhibited in London in 1663.

E. Fischer (1910) has given the history of a family in Upper Alsace, near Colmar, some of whose members were almost entirely devoid of hair. Daniel Bollenbach, belonging to the second generation of the pedigree (see Fig. 38), had no hair of the ordinary type, but his whole head bore a very scattered, soft down, about 1 centimetre long, composed of soft, thin, colourless hairs. Under the microscope they are seen to have no central medulla or pigment granules, to be somewhat thinner than ordinary hair, and twisted. Amongst these are a very few longer (3 centimetres) and somewhat thicker, pale reddish, delicate hairs. Under the microscope these show a normal central medulla and a weak reddish-brown pigmentation. Eyebrows and eyelashes are lacking. The arms and legs are hairless; also there is no breast hair or axillary hair. The nails of the toes and fingers are deformed, becoming thick and rough. The teeth decayed early, leaving many stumps. There is here the well-known correlation between deficiencies in teeth, nails, and hair. Some other members of the family have a few hairs on the body.

The inheritance of this hairless condition shows peculiarities (see chart, Fig. 38), which are difficult to explain except perhaps on an hypothesis of variable or reversed dominance of a single Mendelian factor. The character itself seems to have appeared suddenly through a germinal change, since the two generations preceding its original appearance were all normal, although they included cousin marriages which would probably have brought out a recessive character if it had been present. It will be seen that in the F_1 Mathias, who was normal, had only normal descendants, but Katherine (abnormal) also had only normal descendants through three generations. If the character were recessive its absence here would be explained, since her husband was probably homozygous normal. Maria and Salome, if their husbands (Bollenbach) were heterozygous, should have half their children of each type. The actual numbers were three normals to four hairless, and seven normals to seven hairless respectively. The numbers are, of course, too

* *Animals and Plants*, i. 448.

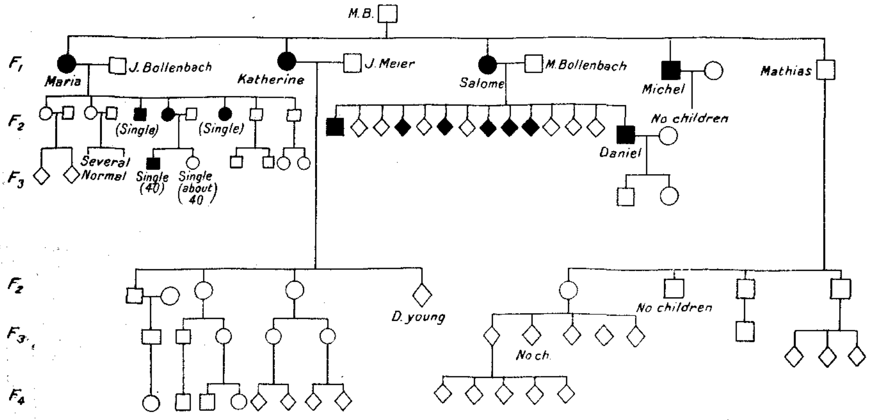


FIG. 33.—PEDIGREE CHART OF FAMILY SHOWING ATRICHOSIS (ABSENCE OF HAIR).

In this and following pedigree charts, black always means the presence of the abnormality, white its absence. The squares are males, circles females, and diamonds of unknown sex. (Chart modified after E. Fischer.)

small to make a certain interpretation, but the most likely interpretation appears to be that the character behaved as a recessive. In the case of Katherine, it is very unlikely that it would fail to appear in any of her four children if it were dominant. The fact that the sex of so many of the children is unrecorded indicates that the records are not, perhaps, very accurate.

Inbreeding does not explain the origin of this character, which was probably due to germinal change, and if the Bollenbachs were homozygous it would behave partly as a dominant. The abnormal section of the family is fast dying out. Sexual selection is apparently a factor, for abnormal members of the family often remain single. Of the fourteen children of Salome, all died but one (Daniel), who had two children, only one of which reached maturity. Michel remained childless. Only two abnormal members of this family remain—both old men. At their death, the abnormality will be lost after fifteen abnormal individuals had appeared in three generations. This is a marked case of an abnormality appearing suddenly and then disappearing in a few generations.

A case of the sudden and complete loss of hair in an individual was described by Wells (1800). A London man thirty-six years of age lost all the hair from his body, including eyebrows and eyelashes, in five or six weeks. He had never had syphilis or taken mercury.

Alopecia or hairlessness in mammals is not uncommon, being known to occur in the horse, cow, goat, dog, pig, rat, mouse, rabbit, and guinea-pig; and various incompletely featherless conditions are known in fowls. Cole (1919) describes a condition occurring in a herd of Holstein-Friesians in Wisconsin, in which certain incisor teeth were lacking or deficient, so that grass could only be eaten with difficulty, and the hair was very short, especially on the neck and head. Five calves of the above type appeared, and the condition seems to be recessive.

A full account of practically complete hairlessness in Swedish Holstein-Friesian cattle is given by Mohr and Wriedt (1928). It is a sublethal recessive gene. By tracing back the pedigrees it was shown that a bull imported from Friesland in 1902 was heterozygous for hairlessness. As he was an imported sire this condition is now widespread in the breed. The calves die a few minutes after birth. They have a smooth, glossy skin, the impregnated areas being pink. There are hairs on the

muzzle and around the eyelids, the ears are normally covered, but there are few hairs elsewhere. The hoofs and teeth are normal. A total of 98 normal to 12-14 hairless calves are reported, where expectation is 7 : 1. The condition of the skin was found to be due to a marked delay in its embryonic development. The development of hair was only about to begin, while the sweat glands were greatly enlarged.

The hairless Chihuahuan dog of Northern Mexico is described (*Journ. Hered.*, viii. 519). It is rare, is very sensitive to temperature changes, and is said to have defective teeth. Hairless × normal gives, at least in some cases, half of each type. Naked dogs have also been known from parts of Asia and Africa. Hairlessness has been reported at various times in different species of mice. Sumner (1924) summarises the literature and describes the hairless mutations which appeared in breeding experiments with different stocks of Peromyscus. The skin is usually corrugated in folds, and they usually die young. Fifty-two hairless descendants were obtained. In crosses the condition was a simple recessive, but there was a deficiency of hairless due to their lesser viability. Hairlessness in rats due to a single recessive factor is recorded by E. Roberts (1924). A practically hairless male wild rat mated with the backcross offspring from an albino female gave in all 22 hairless offspring, the hair falling out after twenty-four days.

Hairless rabbits, again a simple recessive, are described by Kislovsky (1928). They appeared from inbreeding normals and were recognisable at about two weeks of age, DR × DR litters giving 17 normal : 7 hairless. Usually there was hair only on the muzzle, tips of the ears, the back of the legs, and a tuft behind the scapula. Some had defective and some normal teeth, but all died before they were a month old; so the condition was lethal and they could not be bred. In pigs (Welch, 1917) the conditions appear to be different, and the kind of hairlessness accompanied by goitre which occurs in them is due to an enlarged thyroid which is deficient in iodine. This condition, which occurs in pigs, lambs, and calves in goitrous regions of the North-Western States, can apparently be prevented by feeding iodine during the period of gestation.

In fowls, the bare-neck breed was described by Davenport (1914). This is a simple dominant mutation, in which the neck pteryla and certain other parts of the skin are devoid of feathers. Davenport suggested that an anti-enzyme inhibitor is present which prevents the development of the enzyme

normally causing feather-formation. Crew (1922) has further described these hackleless fowls, and Greenwood (1927) points out that the apteria are devoid both of feathers and also of the down and semiplumes which are found on the apteria of normal fowls. The bare skin of the neck is also thickened and congested with bloodvessels, like the comb and wattles. This type is known from Transylvania and also from Barbadoes. Danforth (1928) applies the term alopecia to absence of feathers. In Rhode Island Red fowls a hen appeared with almost full feathering on the head and upper neck, the rest of the body showing deficiency, there being only a few wing feathers, the sides of the body bare, and the tail rudimentary. A piece of skin grafted from a Leghorn produced feathers, indicating that the nakedness was not due to lack of endocrines.

Certain other hair abnormalities in man may be mentioned. *Monilithrix*, or early baldness with the development of moniliform hairs, was a simple dominant in a French family (16 cases in five generations). Gossage (1908) records five such families, dominant, but skipping a generation in one family. In three sibships the numbers were 30 normal : 31 affected. Other families are cited by Danforth (1925). Heuck (1924) finds monilithrix associated with keratosis follicularis in 13 out of 45 cases. The dominance is irregular in some cases, " carriers " being noted in five cases, four of whom were females, but the proportion of diseased to normal was 47 : 46.

Several other pedigrees showing sex-limited inheritance may be cited from a large mass of data furnished by Sedgwick (1863). *Pityriasis versicolor*, a skin disease, is confined to the males, but transmitted by the females to their children in a family where the grandfather, his three sons, and nine males of the next generation all have it. In another family numerous *warts* on the hands characterise the female line for two generations, the mother and her three daughters having them, the two sons normal.

In another family numerous *sebaceous tumours* on the scalp occurred in a mother, her daughter and granddaughter, while the sons were free. The brother's daughters, however, have them, as well as several cousins of different degrees of relationship. Hence the condition can be transmitted through (unaffected) males. This woman's mother, grandmother, and female relations backwards for seven generations were similarly affected. " No female who had attained her tenth year of age was without them, whilst none of the males in the family ever

ıad them." In another family exactly the same manner of nheritance occurred, a woman, the mother, mother's mother, .nd so on, for two more generations, all having scalp tumours, .s well as several female first and second cousins on the mother's ide. Again all the females and none of the males developed he condition.

LITERATURE

ɪNONYMOUS. 1917. The hairless dog. *Journ. Hered.*, viii. 519-520, figs. 2.

ꞁAKER, HENRY. 1755. A supplement to the account of a distempered skin, published in the 424th number of the *Philosophical Transactions. Phil. Trans.*, xlix. 21-24, fig. 1.

ꞁERGLUND, V. 1925. Sechs Fälle von Hypotrichosis in einer Familie. *Hereditas*, vi. 44-48.

ꞁERNSTEIN, FELIX. 1925. Beiträge zur Mendelistischen Anthropologie. II. Quantitative Rassenanalyse auf Grund von statistichen Beobachtungen über den Drehsinn des Kopfhaarwirbels. *Sitzgsbr. d. Preuss. Akad. Wissensch. Physik.-Math. Kl.* Jahrg. 1925. 71-82.

·RUSHFIELD, T., and WYATT, W. 1926. Epiloia. *Brit. Journ. Children's Diseases*, xxiii. 178-185, figs. 7.

ULLOCH, W. 1909. Chronic hereditary Trophœdema. *Treasury of Human Inheritance*, pt. i., 32-38, pls. 2.

·ULLOCH, W. 1909. Angioneurotic Œdema (Quincke's disease). *Treasury of Human Inheritance*, pt. iii., 38-49, pls. 2.

ꞁOLE, L. J. 1919. A defect of hair and teeth in cattle, probably hereditary. *Journ. Hered.*, x. 303-306, figs. 5.

ꞁREW, F. A. E. Hackleless or bare-necked fowls. *Nat. Poult. Journ.*, p. 194.

ꞁANFORTH, C. H. 1921. Distribution of hair on the digits in man. *Amer. Journ. Phys. Anthrop.*, iv. 189-204.

ꞁANFORTH, C. H. 1925. Hair, with special reference to hypertrichosis. *Amer. Med. Assoc.*, pp. 152, figs. 64, also *Arch. Dermat. and Syph.*, 1925, April-October.

ꞁANFORTH, C. H. 1928. A case of alopecia in the fowl. *Journ. Hered.*, xix. 547-550, figs. 3.

ꞁAVENPORT, C. B. 1914. The Bare-necks. *Journ. Hered.*, v. 374, fig. 1.

ꞁAVENPORT, C. B. 1916. The hereditary factor in pellagra. *Arch. Internat. Med.*, xviii. 4-31.

ꞁUERDEN, J. S. 1918. Some results of ostrich investigations. *S. African Journ. Sci.*, Nov.-Dec., pp. 38, pls. 4, figs. 4, tables 10.

ꞁUERDEN, J. S. 1919. Crossing the N. African and S. African ostrich. *Journ. Genetics*, viii. 155-198, pl. 1, figs. 2, tables 10.

ANTHAM, H. B. 1924. Heredity in man: its importance both biologically and educationally. *S. African Journ. Sci.*, xxi. 498-527, figs. 15.

ANTHAM, H. B. 1925. Some factors in eugenics, together with notes on some S. African cases. *S. African Journ. Sci.*, xxii. 400-424, figs. 4.

ASOLD, ANNA. 1924. Studien über Vererbung von Hautkrankheiten. VI Xanthom (Cholesterosis cutis). *Arch. f. Rassen. u. Gesells.-Biol.*, xvi. 54-66.

FISCHER, EUGEN. 1910. Ein Fall von erblicher Haararmut und die Art ihrer Vererbung. *Arch. f. Rass. u. Gesells.-Biol.*, vii. 50-56.

FRIEDENTHAL, HANS. 1908. Das Haarkleid des Menschen. Berlin: F. Fischer, pp. 179, pls. 43.

GOSSAGE, A. M. 1908. The inheritance of certain human abnormalities. *Quart. Journ. Med.*, i. 331-347.

GREENWOOD, A. W. 1927. The "hackleless" fowl. *Proc. Roy. Phys. Soc.*, xxi. 123-129, figs. 4.

HADLEY, F. B. 1927. Congenital epithelial defects of calves. *Journ. Heredity*, xviii. 487-495, figs. 3.

HADLEY, F. B., and COLE, L. J. 1928. Inherited epithelial defects in cattle. *Agric. Exp. Sta. Univ. Wisconsin Research Bull.*, No. 86, pp. 35, figs. 12.

HADLEY, F. B., and WARWICK, B. L. 1927. Inherited defects in live stock. *Journ. Amer. Vet. Med. Assoc.*, xxiii. 492-504.

HARE, H. J. H. 1929. Premature whitening of the hair. *Journ. Hered.*, xx. 31-32, fig. 1.

HAUSMAN, L. A. 1925. The relationships of the microscopic structural characters of human head-hair. *Amer. Journ. Phys. Anthrop.*, viii. 173-177.

HAUSMAN, L. A. 1925. A comparative racial study of the structural elements of human head-hair. *Amer. Nat.*, lix. 529-538, figs. 5.

VON HEINER, L. 1926. Beiträge zur Erblichkeit der Psoriasis. *Dermat. Zeits.*, xlviii. 176-184.

HEUCK, O. 1924. Studien über Vererbung von Hautkrankheiten. VII. Monilotrichosis. *Arch. f. Dermat. u. Syphilis*, cxlvii. 196-200.

HOFMANN, E. 1926. Über den Erbgang bei Epidermolysis bullosa hereditaria. *Arch. f. Rassen. u. Gesells.-Biol.*, xviii. 353-368, figs. 7.

HOPE, W. B., and FRENCH, H. 1908. Persistent hereditary œdema of the legs with acute exacerbations. Milroy's disease. *Quart. Journ. Med.*, i. 312-330, pls. 2.

JENNESS, DIAMOND. 1929. The people of the twilight. New York: Macmillan, pp. 247.

JENNY, E. 1927. Über eine letal verlaufende Form von Epidermolysis bullosa hereditaria beim Säugling. *Zeits. f. Kinderheilk.*, xliii. 138-148.

KISLOVSKY, D. A. 1928. Naked—a recessive mutation in the rabbit. *Journ. Hered.*, xix. 438-439, figs. 3.

LANDAUER, W. 1926. Die vererbung von Haar- und Hautmerkmalen Ausschliesslich Färbung Zeichnung, mit Berüchsichtigung von Rassen-differenzierung und Deszendenz. *Zeits. f. ind. Abst. u. Vererb.*, xlii. 113-224.

LAUTERBACH, C. E., and KNIGHT, J. B. 1927. Variation in whorl of the head hair. *Journ. Hered.*, xviii. 107-115, figs. 4.

LEVEN, L. 1927. Scheckung der Haut und Flecking der Zähne. *Klin. Wchnschr.*, vi. 904-906.

LUNDBORG, H. 1926. Geschlechtsgebundene Vererbung von ichthyosis simplex (vulgaris) in einer Schwedischen Bauernsippe. *Hereditas*, ix. 45-48.

MACHIN, J. 1733. An extract from the minutes of the Royal Society, March 16, 1731, containing an uncommon case of a distempered skin. *Phil. Trans.*, xxxvii. 299-301, figs. 3.

MANSON, J. S. 1928. Observations on human heredity. London: Lewis, pp. 84, pls. 8, figs. 19.

MARTIN, P. J. 1818. Case of hereditary ichthyosis. *Med.-Chirurg. Trans.*, ix. 52-55, pls. 2.

MEIROWSKY, E., and BRUCK, W. 1921. Über die Vererbung und die Aetiologie der Muttermäler. *Münch. med. Wchnschr.*, lxviii. pt. 2, 1048-1049.

MEIROWSKY, E., and LEVEN, L. 1921. Tierzeichnung, Menschenscheckung und Systematisation der Muttermäler. Berlin: Springer, pp. 79, pls. 19.

MOHR, O. L. 1926. Über Letalfaktoren mit Berücksichtigung ihres Verhaltens bei Haustieren und beim Menschen. *Zeits. f. ind. Abst. u. Vererb.*, xli. 59-109, figs. 10, pl. 1.

MOHR, O. L., and WRIEDT, C. 1928. Hairless, a new recessive lethal in cattle. *Journ. Genetics*, xix. 315-336, pls. 2, fig. 1.

ORBAN-VADJA, A. 1925. Familiäre Ichthyosis. *Zbl. f. Hautkrankh.*, xvii. 627.

OSBORNE, DOROTHY. 1916. Inheritance of baldness. *Journ. Hered.*, vii. 347-355, figs. 9.

PICK, E. 1925. Familiäre ichthyosis. *Zbl. f. Haut. u. Geschlkh.*, xvi. 521.

ROBERTS, ELMER. 1924. Inheritance of hypotrichosis in rats. *Anat. Rec.*, xxix. 141.

SCHWARZBURG, W. 1927. Statistische Untersuchungen über den menschlichen Scheitelwirbel und seine Vererbung. *Zeits. f. Morph. u. Anthrop.*, xxvi. 195-224, figs. 6.

SEDGWICK, W. 1861. On sexual limitation in hereditary disease. *Brit. and Foreign Med.-Chirurg. Rev.*, xxvii. 477-489, xxviii. 198-214.

SEDGWICK, W. 1863. On the influence of sex in hereditary disease. *Brit. and Foreign Med.-Chirurg. Review*, xxxi. 445-478, xxxii. 159-197.

SIEMENS, H. W. 1925. Über einen in der menschlichen Pathologie noch nicht beobachteten Vererbungsmodus: dominant-geschlechtsgebundene Vererbung. *Arch. f. Rass. u. Gesells.-Biol.*, xvii. 47-61, figs. 5.

SIEMENS, H. W. 1926. Die Vererbungspathologie der Akne. *Münch. med. Wchnschr.*, lxxiii. 1514-1517.

SIEMENS, H. W., and KOHN, E. 1925. Studien über Vererbung von Hautkrankheiten. IX. Xeroderma pigmentosum (mit Mitteilung von 5 neuen Fällen). *Zeits. f. ind. Abst. u. Vererb.*, xxxviii. 1-61.

SUMNER, F. B. 1924. Hairless mice. *Journ. Hered.*, xv. 475-481, figs. 3.

TROTTER, M., and DANFORTH, C. H. 1922. The incidence and heredity of facial hypertrichosis in white women. *Amer. Journ. Phys. Anthrop.*, v. 391-397.

WEHEFRITZ, E. 1924. Zur Vererbung der Ichthyosis. *Zeits. f. Konst.*, x. 394-400.

WELCH, H. 1917. Hairlessness and goiter in new-born domestic animals. *Univ. Montana Agric. Exp. Stn. Bull.* No. 119: 83-104, figs. 9.

WELLS, W. C. 1800. An instance of the entire want of hair in the human body. *Trans. Soc. Med. and Chir. Knowledge*, ii. 264-267.

WIENER, KURT. 1925. Gummihaut (Cutis laxa) mit dominanter Vererbung. *Arch. f. Dermat. u. Syph.*, cxlviii. 599-601.

CHAPTER VIII

ANATOMICAL ABNORMALITIES OF THE HANDS, FEET, AND LIMBS

ALMOST every conceivable and many unbelievable abnormalities of an anatomical nature are known to be inherited. Some of these are deficiencies of the skeletal development as a whole or of certain parts of it. Others refer to particular organs which may be absent or malformed. The classification of these abnormalities is a matter of some difficulty, as many of them refer to more than one organ system; some pertain to a single minor or even minute point of structure and others to a whole organ system.

Probably more abnormalities are known of the hands than of any other part of the body except the eye. There are also certain inherited differences in shape and structure of the hands and feet which are in no sense abnormalities.

SPLIT HAND AND FOOT, or "lobster claw," is a relatively common abnormality. I am indebted to Professor C. G. Seligman for the following reference to negroes with "crab claw" in Guinea. The quotation* is from Hartsinck, who wrote in 1770, and who gives an illustration of the condition described. "Regarding the 'Touvingas,' or two-fingered negroes, it is observed that they are a people who had only two large fingers on their hands and two large toes on their feet, similar to those of a crab, as is figured in the illustration. The wrist is somewhat larger than that of the average man: the thumb and little finger are more than twice the usual size, and stand out from the limb, have a bend at the tip, and appear as one piece of flesh on which there is something like a nail. The palm of the hand has no bends, but appears as a solid mass, yet the divisions can be felt. . . . After the declaration of freedom, these negroes of Saramacca walked publicly through Paramaribo. . . . Many argue that they are not a distinct tribe or nation, but just a family who by accident or freak of nature have been thus

* In Bureau of Amer. Ethnology, 1911-12, Report No. 153, W. E. Roth, "Animism and Folk-lore of Guiana Indians," p. 364.

deformed. These people are becoming very rare indeed, probably through intercourse with others, fast bastardising."

This very likely represents an independent origin of the condition in negro slaves. Their numbers are unfortunately not stated, but must have been considerable if they were regarded as an independent "tribe" or "nation."

Lewis and Embleton (1908) consider a collection of 180 cases of this deformity. Many varieties of the condition occur. In the "G" family, to which many of their data refer, the hands are variously misshapen, and each foot consists of two toes separated by a deep cleft. Rarely the toe on one side may be double, and the toes are generally bent claw-wise at their extremities. Both the hands and feet of these people are said to have great functional capacity and accuracy in use, including needlework and handwriting. The variations in the deformity are only in degree. Rarely one or both hands may be normal when the feet are split. The condition may also be associated with syndactyly (fused fingers) or polydactyly (extra fingers or toes). Cross bones frequently occur in the hands, but never in the feet. The inheritance is essentially that of a Mendelian dominant, though the expected ratios are not always adhered to.

In the "G" family this condition has been traced through five generations. It never skips a generation, and derived normals × normals give only normal offspring. It is transmitted equally through either sex. In the offspring of crosses between deformed and normals, Lewis and Embleton find a total of forty-four deformed to thirty-two normal. In some, though not all, of the other data of inheritance of split-foot, they find a similar excess of deformed individuals, which appears to be significant. It does not necessarily follow that the condition is not represented by a single difference in the germ plasm. Indeed, they agree that it has arisen as a "sport" or mutation of germinal origin. They state "there are records of over thirty instances of the origin of this same sport," and account for this by the now widely accepted view that mutations tend to occur and recur in definite directions. Since the character is dominant it cannot remain hidden in the germ plasm, but must appear externally if the germ cell containing it develops into an individual.

All writers agree that this character segregates sharply, but Lewis and Embleton claim that it "does not follow the laws of Mendel," because of the excess of abnormals in the

offspring of crosses with normals. This does not necessarily follow, for it is now known that many physiological and environmental conditions may cause distortion of Mendelian ratios. Lewis and Embleton believe there is a "decided tendency for the deformity to die out" in later generations. They appear to think that this results from the germinal condition representing split-foot becoming unstable. Probably the struggle for existence has something to do with it, as well as sexual selection.

Pearson (1908) refers to the evidence for the existence in Scotland of a family, "the Cleppie Bells," with a deformed hand inheritance extending over two centuries. He traces the deformity in another family for four generations, and finds again an excess of abnormals in the offspring of crosses with normals (25 : 14). He concludes: "On the whole, while these cases give very definite evidence of the segregation factor, they do not seem to me to favour the segregation in rigid Mendelian proportions." The stock of this family is otherwise normal, and they have no difficulty in finding normal mates. The gait is ungainly, but the children at school hold their own in writing, drawing, and needlework. Additional data for this family are given by McMullen and Pearson (1913), the numbers of abnormals recorded having increased from twenty-five to thirty-three. In the third generation the result is in conformity with the Mendelian expectation of equality of normals and abnormals. In the fourth and fifth generations there is a total of twenty-eight affected to thirteen normal.

Everything considered, it seems most reasonable to regard this condition as due to a single Mendelian dominant factor which arises from time to time as a mutation, but which, through increased viability or for some other reason, occurs in more than 50 per cent. of the offspring from crosses with the normal. Lewis (1909*a*) records certain other split-foot pedigrees. The only facts that need specially concern us are: (1) a family of ten, in which half are abnormal and half normal; (2) a family of six, all abnormal. In the latter the father may perhaps have been homozygous.

Fetscher (1922), on the other hand, describes pedigrees in which CLUB-FOOT, a related abnormality, is obviously recessive, although more than one factor may be concerned. Various writers find that it has a frequency of about 1 in 1,000-1,600, and commonly occurs in the offspring of normal parents. From a study of 186 patients in 25 family groups, Fetscher finds,

in conformity with earlier ratios, that the sex-ratio of affected individuals is 67♂ : 33♀ or 2 : 1. He finds that in club-foot (pes varus congenitus) × normal, 11 per cent. of children have club-foot, whereas with a single factor and no other disturbances the expectation would be 50 per cent. Similarly in normal × normal from club-footed parents, 5·3 per cent. of children (not 25 per cent.) were affected. Fetscher concluded that half to three-quarters of the cases of club-foot are heritable, due to a nervous derangement, and that the other cases have no single cause, but may result from bone defects, uterine anomalies, or from multiple births. He develops an elaborate and highly improbable theory based on non-disjunction of chromosomes to account for the inheritance. In the various pedigrees are numerous associated defects, including microcephaly, dwarfism, mongolism, deaf-mutes, cleft-palate, idiocy, epilepsy, hysteria, and suicide.

Müller (1926), in an important study with an extensive bibliography, points out that it was recognised a century ago that club-foot resulted from spastic muscular contraction, the bones being drawn out of their proper positions. Since then two explanations of its pathogenesis have been discussed: (1) a germinal deficiency; (2) from external pressure on the normal foot. In the terminology of Siemens (1923), it may be an idiovariation or it may be paratypic, due to an inhibition of development. Most recently club-foot has been viewed as a neurogenic or myogenic deformity, caused by malformation of the caudal end of the spinal cord, or dystrophy of the leg muscles, of purely peripheral origin. It is clear that a series of conditions of very different ætiology and anatomical structure are included under the term club-foot. Müller examined 358 cases. The condition is classified as of three types: (1) pes varo-supinatus, 61 per cent.; (2) pes varo-excavatus, 24·8 per cent.; (3) pes varus, 14·2 per cent. He circulated a questionnaire regarding inheritance and got replies from 262. It is clear from the results that, like so many human abnormalities, the methods of inheritance are various, as shown by the 40 pedigrees, in which there are many irregularities and frequent skipping of a generation. The following types occur: (1) Unilateral club-foot, inherited always on the same side or changing between right and left; (2) symmetrical, always in both feet; (3) changing between unilateral and symmetrical (four pedigrees). One pedigree shows dominant club-foot on both sides through four generations. Dominance occurs probably in

9 of the pedigrees, in 29 there is no dominance. The dominant pedigrees are all pedes varo-excavati, two of them unilateral, seven bilateral. Among the apparently recessive pedigrees, both varo-supinati and varo-excavati occur (the latter only in six pedigrees). In one family the eldest son had club-foot at birth, while others developed it during childhood. The appearance of club-foot after birth is rare (1 per cent.) in supinati, but common (23·5 per cent.) in excavati. In two pairs of apparently identical twins, one had bilateral club-foot, the other was normal. This would represent presumably a non-inherited type.

FIG. 39.—BRACHYDACTYLOUS AND NORMAL HANDS FOR COMPARISON. (After Drinkwater.)

In very young children the club-feet are almost invariably supinated, and this can change during development to varo-excavatus. The percentage of inheritance of varo-excavati is twice that of supinati, and they show a normal sex-ratio. Twenty per cent. of all cases of club-foot, or 15 per cent. of congenital club-foot, Müller concludes is of the recessive type—not a simple recessive, but either involving polymery or due to an inherited disposition to club-foot being suppressed by paratypic conditions. The largest group is that in which neither heredity nor abnormal intra-uterine conditions can at present be shown. In the undoubtedly inherited cases the sex-ratio of club-footed is 2 : 1, and as the doubtful group above mentioned has the same ratio they probably also come in the

inherited class. Spina bifida, which is fatal in its effects, appears frequently with club-foot.

BRACHYDACTYLY is an abnormality which has been even more studied in recent years, although it is much less frequent in its occurrence than split-foot or club-foot. The condition is illustrated in Fig. 39, which shows normal and brachydactylous hands for comparison, and Fig. 40, which is a radiogram

FIG. 40.—RADIOGRAM OF A BRACHYDACTYLOUS HAND, SHOWING THE TWO PHALANGES IN EACH FINGER. (After Drinkwater.)

showing the bones of a brachydactylous hand. The earliest study of the inheritance of brachydactyly was by Farabee (1905) in an American family from Pennsylvania. He shows that the condition was inherited as a simple Mendelian dominant, the offspring of the affected mated with normal giving 50 per cent. of each type (thiry-six affected, thirty-three normal). Brachydactylous women cannot play the piano well owing to their inability to span the octave. Brachydactylous

men in this family include farmers, mechanics, business men, and school teachers. One was head of a commercial school and a fine penman, another was a baseball catcher. The arms and legs are short, but the sitting-height is nearly normal, and abnormals are stouter than their normal sibs.* There is an unverified tradition in the family that the first member with short fingers came from Normandy in the army of William the Conqueror. Brachydactylous individuals have never intermarried; but the abnormals always marry first, and will soon have gained a generation in this way. This was the first case of Mendelian inheritance demonstrated in man.

Drinkwater (1908) independently investigated a British family, with the same results as regards inheritance. He found that the strength of grip in brachydactylous individuals was considerably below the average. They complain that they cannot play the piano or any other musical instrument requiring normal length of fingers, their grasp of objects is smaller than normal, and the women cannot do netting. That they are handicapped is shown by the fact that their social position is lower than that of their normal relatives. They are engaged in unskilled labour, while their normal relatives include farmers, grocers, etc. In a wild tribe where personal defence with weapons is a necessity, brachydactylous individuals would probably not survive.

In several papers Drinkwater has made a careful anatomical investigation of brachydactylous hands and feet, including radiographic studies. The condition applies equally to fingers and toes, and is accompanied by short stature. In the digits he showed that the middle phalanx is very short, and has become ankylosed to the base of the terminal phalanx. Hence the second phalanx is rudimentary, and at a certain stage of development it unites with the terminal phalanx. The most important feature is the absence of the epiphysis (terminal cartilage, which becomes ossified) at the base of the second phalanx. The epiphysis may also, perhaps, be missing in some cases from the third phalanx, the second and third phalanges consisting at first of a single piece of cartilage. The metacarpal (hand) bones are also more or less abnormal, but the metatarsal (instep) bones are unaffected. This abnormal family was very prolific, the number of children in nine families averaging eleven each A normal woman had forty-five descendants,

* That is, brothers and sisters.

while a brachydactylous woman in the same family had ninety-nine descendants. The numbers in successive generations show that the condition is on the increase, and that there is no chance of it becoming extinct so long as the brachydactylous members continue to marry. For some unknown reason they do marry more frequently than their normal sisters.

The essential feature in brachydactyly is, then, the absence of the epiphysis at the base of the second phalanx, with subsequent ankylosis of the second and third phalanges. The fingers are about half the normal length. Although brachydactylous individuals are lacking in some forms of dexterity, and therefore must accept a lower social status, yet they show a decided increase in fecundity compared with normal members of the same family. In this family twenty-five now living in England and Wales are brachydactylous. Beginning with the fourth generation, the total number of descendants from DR × RR* crosses is seventy-five, of whom thirty-nine are abnormal.

No connection could be traced between Drinkwater's first brachydactylous family and the one described by Farabee, there being no surname common to the two families. Drinkwater (1915) has since described another family, however, which he has shown to be descended from a member of Farabee's family, who removed from America and settled in this country. In this family and its American antecedents the abnormality can be traced for six generations. In both branches of this family the proportion of females among the abnormals is exactly 61 per cent. In the English branch fifty abnormals were recorded to forty-eight normals, where 50 per cent. of each type were expected, showing that heterozygous brachydactyls produce the two types of germ cells in equal numbers. Normals mated together invariably have only normal offspring. The shortness of stature of brachydactyls is shown to be due to the short legs, both femur and tibia being shorter than in normal members of the family.†

Drinkwater has also described in two families the condition

* D = dominant, R = recessive, hence DR is a heterozygous dominant, and RR pure (homozygous) recessive.

† That brachydactyly and other abnormalities are found in the Chinese is shown by Droogleever Fortuyn (1927), who describes human embryos in the collection of the Peking Union Medical College showing brachydactyly, syndactyly, cleft-palate, ectopia cordis, osteomalacia, spina bifida, exencephaly, anencephaly, etc.

which he calls MINOR BRACHYDACTYLY (1912, 1914). In a Lancashire family this abnormality has been traced through five generations, and sixteen abnormals were living when the study was made. The fingers are less shortened than in brachydactyly, but the middle phalanx of each finger is abnormally short. This is partly due to the absence of the epiphysis from the base of the second phalanx, except in the middle finger, and also to a slight shortening of the second phalanx, but is chiefly due to the fact that the cartilage between the shaft and the epiphysis becomes prematurely ossified, thus causing cessation of growth in length of the fingers at an early age. Ankylosis of the epiphysis and the second phalanx frequently occurs earlier in the first and fourth fingers than in the second and third, thus leading to a greater shortening of the former. The abnormality of the toes is practically identical with that in ordinary brachydactyly. This family is also shorter in stature. As in the brachydactylous family, the women are $4\frac{3}{4}$ inches and the men 8 inches shorter than their normal siblings. A total of twenty-one abnormals to twenty-six normals was recorded in families having one abnormal parent. The abnormals in this family are said to have better health than the normals. In the children the abnormality is inconspicuous, and is sometimes detected only by flexing the finger.

In the second family showing minor-brachydactyly (Drinkwater, 1914), the conditions closely resemble those in the previous family, but so far as the records go back there is no connection. It is found in five generations, there being nine abnormals to ten normals, eight of the former now living. They are all descended from an illegitimate daughter of a short-fingered man, the mother having been married to a normal man by whom she had entirely normal descendants. These forms of brachydactyly are, therefore, all simple Mendelian dominants, but they show no appreciable excess of abnormals in inheritance, and they show a clear tendency to increase rather than die out, notwithstanding their social handicap, or possibly on account of it. Bateson, who discussed the earlier records of brachydactyly (1909, p. 210), refers to a four-generation pedigree, described by Walker, of what appears to be a mild form of minor-brachydactyly inherited in the same way.

Lewis (1909*c*), in a thesaurus of the results of the study of brachydactyly, up to the time his paper appeared, cites two other cases with interesting features. In Mercier's case a French family is described in which eighteen members in three

generations are brachydactyl, having two phalanges on all the fingers and toes. Hasselwander's case (a German family) presents a feature of special interest. There were six abnormal members of the family in three generations. The original brachydactyl of this pedigree came from normal parents. His advent must, then, mark an independent origin of the condition through a mutation, unless possibly his affected parent only had the condition in a slight degree, and so was mistaken for a normal. The actual origin of such a case is naturally difficult to prove, and this can only be done where the conditions in

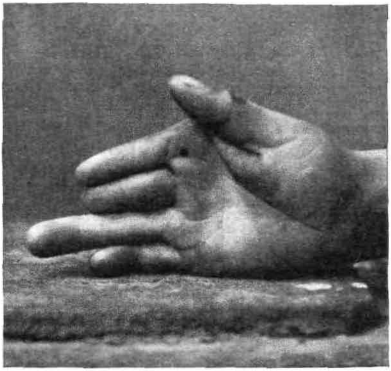


FIG. 41.—HAND SHOWING ABNORMAL SEGMENTATION OF THE INDEX AND MIDDLE FINGERS. (After Drinkwater.)

both parents and grandparents are accurately and certainly known from observation to be normal.

That various other modifications of typical brachydactyly, in addition to those described above, are inherited in the same way is shown by such records as those since published by Dr. Drinkwater (1916), whose accurate work in recording these cases is of great value. He traces through four generations a case of abnormal segmentation of the index and middle fingers, the third finger being much longer than any of the others owing to the great length of its proximal phalanx. The first and

second fingers are also more or less tilted away from the thumb (see Figs. 41 and 42). There are thirty-six descendants of the abnormal members of the family, fifteen of whom show the abnormality. The feet in these individuals show ordinary brachydactyly. From a careful study of radiographs the following anatomical interpretation emerges : The index finger has at its base an extra triangular bone which sets the finger obliquely

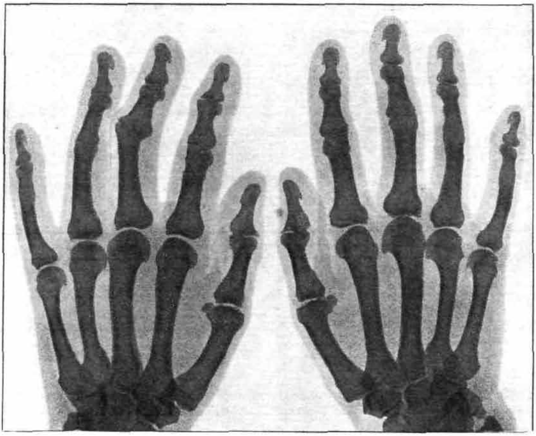


FIG. 42.—RADIOGRAPH OF THE TWO HANDS OF A GIRL AGED NINETEEN, IN THE SAME FAMILY AS FIG. 41. (After Drinkwater.)

to the hand. The proximal phalanx of the middle finger appears to be divided equally or unequally into two parts; the lower part, however, is probably an extra bone corresponding to that in the index finger, and it also is set somewhat obliquely. In the adult hand these extra bones become ossified with the proximal phalanx of the corresponding finger. Another peculiarity in this pedigree is the abnormally great length of the proximal phalanx of the ring finger. All these anatomical features behave as a unit in inheritance, with

remarkably little variation in their development so far as observed.

Drinkwater (1917) has described yet another digital abnormality closely related to brachydactyly, which is remarkable for the number of generations for which it is known to have been handed down in one family. It is now called SYMPHALANGISM. The peculiarity is as follows, as found in the hands of a gentleman, A. T., of the present generation: In the middle finger the joint between the middle and basal phalanges is only very

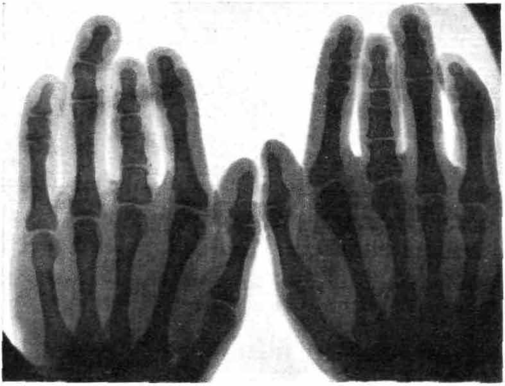


FIG. 43.—SKIAGRAM (PHOTOGRAPH BY RÖNTGEN RAYS) OF THE HANDS OF A. T., *SHOWING* CONTINUITY OF THE PROXIMAL AND MIDDLE PHALANGES IN THE RING AND LITTLE FINGERS. (After Drinkwater.)

slightly movable, the articular surfaces of the bones being enlarged, while in the ring and little fingers there is no joint between the proximal and middle phalanges, these two being completely fused into one (see Fig. 43). All the fingers are movable at the distal joint, and both hands are alike. All the toes, except the hallux, are affected exactly like the ring and little fingers. This man's father and *his* mother are known to have had precisely the same abnormality. His father married twice, and one of the half-brothers shows it. The most interest-

ing feature of this case is that A. T. is a direct descendant in the male line from John Talbot, the first Earl of Shrewsbury, who figures in Shakespeare's *Henry VI.*, and was killed in battle near Bordeaux in 1453. Tradition has it that his thigh bone was broken while on horseback, and that when he fell from his horse he was killed by the blow of a battleaxe on the head. His body was buried in a tomb inside the church at Whitchurch, which was surmounted by a stone effigy. In 1874 the tomb was opened and repaired by one of his descendants. The skeleton was identified by the cleft skull and the fracture of the right thigh bone. The finger bones, when examined, showed the same ankylosis that exists in his modern descendant. On the stone effigy the fingers, which were somewhat damaged, also showed precisely the same thickening of the middle joint as described in his descendant. Clearly, then, this defect has been handed down for more than 500 years as a Mendelian dominant, and the genealogy of the family shows that it must have been inherited through fourteen generations. This, I believe, is the longest period on record for the tracing of an anatomical abnormality in man, though the Hapsburg jaw extends back equally far.

In America, Cushing (1916) has described essentially the same condition, but no connection with the English family can be traced. The condition in this family closely resembles, or is identical with, that in Walker's Maryland family (see p. 148), though no relationship between them has been traced (see also p. 153). Those who have it are commonly spoken of as "straight-fingered," because the fingers can only be partly closed on the palm. The terminal joints can be flexed, although the rest of the finger is straight, and this is true (Hefner, 1924) of the normal fingers on an affected hand, indicating that a co-ordinated muscular change has taken place. In Walker's family there is complete absence of the proximal joint in all except the index fingers, in which there is a trace of a joint. In this finger slight movement is possible, but the middle phalanx is very short. The greater effect on the middle phalanges is true also of Drinkwater's minor-brachydactyly, and is probably due to the fact that the ossification centres appear later in this phalangeal row, this being the last row to ossify and the terminal row the first. The toes are likewise affected, even occasionally, as in "lobster claw," when the hands appear normal. It is quite probable, according to Cushing, that the articulations between the proximal and middle rows of pha-

langes are the last to be laid down, and that "an inhibitory influence checks their development at a stage a few days later than that which checks the formation of the ossification centres and produces brachydactyly." Hence both are conditions of arrested development in different degree. According to Cushing, long slender fingers (dolichodactyly) may result from deficiency of pituitary secretion, while excessive secretion produces short, stubby fingers.

The original member of this "straight-fingered" family, William B., migrated from Scotland to Virginia in 1700. He married, and from him are descended seven generations, most of whom still live in the same region of Virginia. A member of the fifth generation has communicated with a Scottish relative who shows the trait. The inheritance is that of a Mendelian dominant, the family including 452 individuals in eight generations. Of the 150 children of an affected parent in twenty-eight completed families, seventy-eight of them, or 52 per cent., carried the trait. There is considerable variation in the expression of the character, and it may be transmitted in extreme form by a parent who appears to be but slightly affected. In one case a woman who was doubtfully abnormal, but transmitted the trait, was shown by radiogram to have the condition only on the little finger of one hand.

Another family with the same peculiarity of fingers, which cannot be flexed properly, is described by Duncan (1917). It is perhaps related to Cushing's family, since its ancestors are said also to have come from Scotland. The second joints of the fingers, and frequently also of the toes, are perfectly inflexible. The character is a Mendelian dominant and is traced through four generations, the original affected parent (male) being apparently heterozygous.

Rochlin (1928) cites from the literature several other cases of the inheritance of stiff fingers with ankylosed finger joints, and describes a family with seven cases in four generations. Typically the middle joints of digits II to V on both hands were affected, as shown by radiograms; but there were variations, and the toes might also be affected. The condition is a non-sex-linked Mendelian dominant and presumably arose as a mutation.

Symphalangy has been described (Hefner, 1924) in a family from Ohio, dating back to the American revolution and showing a dominant inheritance with 23 cases in six generations. The original ancestor, Joseph B., and his wife emigrated from

Virginia, whence Walker's family also emanated. Dr. Cushing believes that Joseph B. is a grandson of the William B. in his pedigree, and thus these two pedigrees are connected. Probably also Walker's family belongs to the same stock, and quite possibly all trace back to the Earl of Shrewsbury's line, so that the mutation would have happened but once. In Hefner's pedigree, the sibs from DR × RR matings number 22 with fused joints : 27 normal. The ankylosis shows some variation; all four fingers may be affected or only the little finger, and in one individual the condition was only present on one hand. Affected persons were flat-footed, but the toes were normal. Inman (1924) briefly describes another family from Ohio with 4 cases in four generations of direct descent. In the case examined, the fingers were not shortened and the symphalangy occurred in digits II. and V. of both hands, also in digits II.-V. of both feet.

Another pedigree of a short-fingered family is given by Mohr and Wriedt (1919), who review the literature of brachydactyly. The case they describe, with numerous photographs and radiographs, is of a Norwegian family, some of whose members migrated to North America. The malformation consists in a shortening of the second phalanx of the second fingers and toes only, and is called brachyphalangy. There is no shortening of the stature. The condition occurs in two degrees : (1) so slight as to be often overlooked or even invisible; (2) more extreme, probably due to the presence of a modifying or intensifying factor. The inheritance is that of a simple Mendelian dominant. It has been traced through five generations of descendants from a brachyphalangous woman born in Norway in 1764. Detailed knowledge of the earlier generations is obtained from a carefully kept "family book." In two lines descended from an affected daughter and an affected son of this woman, every individual is recorded. In one case intermarriage within affected lines apparently produced an individual homozygous for the character. She was a cripple without fingers or toes, and died at the age of one year, being unable to develop. This shows how serious even a slight abnormality may become if present in the homozygous condition. It corresponds with many of the lethal factors known in *Drosophila*. The writers refer to Mackinder's (1857) record of a family, in which brachyphalangy combined with hypophalangy (less than five fingers) was transmitted for six generations in the manner typical for a Mendelian dominant character.

This was in 1857, before even Mendel's original work was done.

Cragg and Drinkwater (1916) describe a much more extreme case, which Mohr and Wriedt refer to as hypophalangy combined with brachyphalangy. There is an entire absence of the distal phalanges from all digits except the thumb and big toe, and an extremely abortive condition of the middle phalanx in the same digits. Nails are absent. The condition was traced as a Mendelian dominant through five generations, including twenty-seven affected individuals. In six of these there was also a bifurcation of the thumbs, which may be due to the presence of a dominant modifying factor. Wegelin (1917) traces through three generations an abnormality affecting only the little fingers. The terminal phalanx is bent to the radial side, the middle phalanx shortened, and its distal end oblique. It is dominant, but there were fourteen abnormal to two normal in the third generation.

The remarkable accuracy of the inheritance of many digital malformations is shown incidentally by a paternity case (Mohr, 1921), in which the alleged father had a pronounced brachyphalangy affecting the second row of phalanges on fingers and toes II., III., and IV. The thumbs were normal, but the basal phalanx of the great toe was shortened. The hands and feet of the child showed exactly the same malformation, and radiographs indicated absolute correspondence in the bones. The man was therefore adjudged to be the father.

There is an early record* of a peculiar form of brachydactyly in which the mother and two children, who were examined at Uxbridge, had normal thumbs, but the fingers had only one phalanx each, except the ring finger of the left hand, which had two phalanges. There were no nails on these fingers. All the rest of the family were said to be the same, and the condition was stated to have been inherited for nine *previous* generations, but there are no records to substantiate these statements. The character was only transmitted by the women, who sometimes had a child with perfect fingers.

In another case (Rieder, 1899) the father had a rudimentary (short) fourth metacarpal bone, the ring finger being also short and small. The daughter exhibited "lobster claw" in the right hand, while the feet showed absence of certain toes, reduction of certain phalanges, and syndactyly. Such com-

* *Edin. Med. and Surg. Journ.*, 1808, iv., 252.

bined abnormalities in a line of descent are not infrequent. Stieve (1916) describes a case in which the thumbs of both hands have an extra joint. He cites 39 cases from the literature in which there is a supernumerary phalanx on both thumbs, and 16 in which it is on only one. In 33 cases of the former condition, occurring in ten different families, the condition is known to be inherited, while there is no evidence of its inheritance when it occurs on only one hand.

Danforth (1919*a*) describes a condition which he calls brachydactyly in fowls. Such birds differ from the normal in that digit IV., instead of having five phalanges and being longer than digit II., varies from as long as II. (not longer) to a toe having only two phalanges and no nail. He treated with alcohol (1919*b*) fowls which were heterozygous for brachydactyly, polydactyly (extra toes), and white colour—both males and females, the alcohol being inhaled for short periods. A larger percentage of brachydactylous birds was consistently obtained in the offspring of treated males, indicating that germ cells carrying brachydactyly were more resistant than normal germ cells, or possibly (though this is very unlikely) that alcohol damaged the spermatozoa so as to produce the defect. This experimental method should be applicable to a variety of cases, and furnish evidence of the relative viability of different types of germinal differences. Ultimately it might lead to a method of selectively eliminating certain undesirable types of germ cells. The studies of Pearl on the effects of alcohol on pure races of fowls, of Harrison with moths, and some other similar results, indicate that in such cases there is a selective weeding out of weaker germ cells, leaving the stronger to take part in development.

Pol (1921) has made an extensive anatomical investigation of brachydactyly and related digital abnormalities, such as clinodactyly. The latter he regards as an intermediate step between biphalangy and triphalangy. He finds that these anomalies can be classified into two types, differently inherited. In brachyphalangy and hypophalangy only the malformed transmit the deformity—*i.e.*, it is a Mendelian dominant, while in brachyhyperphalangy the transmission is also from normals (hence recessive or showing variable dominance).

Gilmore (1927) describes a family (Fig. 44) with a brachydactylous condition very similar to those previously described. There are only two phalanges in each finger, the proximal ones being of normal length, the distal ones abnormally short.

The nails are rudimentary, not extending to the ends of the fingers. The thumbs had only one phalanx, with a shortened nail. The feet were normal. A labourer suffered no disability from this condition. The inheritance is clearly that of a Mendelian dominant.

Chilton (1927) describes a pedigree with 6 cases in four generations, in which the middle and terminal phalanges were shortened, and each finger had two nails side by side separated by a strip of ordinary skin. The thumbs show the condition most completely and the little fingers least. The feet were normal. The inheritance is that of a simple dominant.

Hereditary SHORTNESS OF THUMBS was first described by Breitenbecher (1923) in a family in Oklahoma. The terminal phalanx of the thumbs is very short with a very broad and short nail, and measurements show that the second phalanx of the

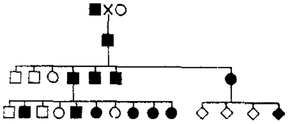


FIG. 44.—PEDIGREE OF A BRACHYDACTYLOUS CONDITION. (After Gilmore.)

other digits is also shorter than normal. The metacarpals, however, are longer than in normal hands. Women with such short thumbs found it necessary to use a short needle in sewing. The condition is traced as a simple Mendelian dominant through five generations. Nine of the children died in infancy. Of the remainder, twelve are seen to be abnormal and fifteen normal, in sufficient agreement with the expected 1 : 1 ratio in a DR × RR cross where the condition of short second phalanges is dominant to normal.

Hoffman (1924) has described apparently the same hereditary conditions in two others. Thomsen (1928) describes the short thumb in Sweden as due entirely to shortening of the distal phalanx, owing to too early ossification of the epiphysis in this phalanx. The nail again is very broad and short, and the condition is not associated with long and narrow hands. Thomsen reports it in fifteen "unrelated" families and agrees that it is dominant in inheritance, but he found exceptions in which a person phenotypically normal could transmit it. The condition may also appear in only one thumb.

Short thumbs similar to those of Breitenbecher's pedigree appear to be of fairly common occurrence. They stand on the border line between an abnormality and the normal condition. Hefner (1924) finds a short terminal phalanx of the thumb in nine separate lines in Ohio and gives three pedigrees of the condition, one with 15 cases in five generations (Fig. 45), and two others each with 4 cases in two generations. The condition sometimes occurs in only one hand. In one individual it was sporadic, his four sibs, parents, grandparents and numerous aunts, uncles and cousins all being supposedly free from it. This may be a case of mutation, but requires fuller investigation before being accepted as such. Hefner also refers to a case where father and son have a peculiar condition of the little finger, which cannot be straightened, apparently owing to shortness of the tendon. The proximal phalanx is also bent at the tip.

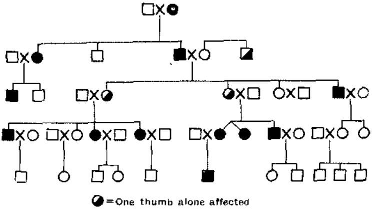


Fig. 45.—Inheritance of Short Thumbs. (After Hefner.)

An abnormality of the nails to which various names have been given is described by A. G. Wilson (1905) as HYPERKERATOSIS OF THE NAIL-BED. The nail is raised above its bed by a horny dark mass secreted under it. The condition begins at birth and persists. The hair and skin are normal. This condition was dominant, with 7 cases in three generations. Exactly the same rare dominant condition of the nails was more fully described by Murray (1921) in another family with 7 cases in three generations. The nails on hands and feet are normal at base, but at the free end they are raised by the horny secretion under them. This is especially marked in the hands. In this pedigree the condition was accompanied by the presence of two or more erupted incisors at birth. These teeth decayed

and disappeared about the sixth to the ninth month. The nails frequently had paronychia (whitlow), but the skin showed neither keratosis, ichthyosis nor psoriasis. Clemente (1928) describes the same condition in a Filipino family (Fig. 46). The interesting feature of this pedigree is that the parents and grandparents and other relatives of III. 7 were normal. The condition must therefore have originated with him as a mutation unless it is a case of illegitimacy. Since half his children show it, he must have been heterozygous and the condition a dominant. The nails were so thickened as to be almost cylindrical at the free tip, and the thick nails on the toes caused a peculiar gait. They were allowed to grow long like claws because cutting them was a painful process.

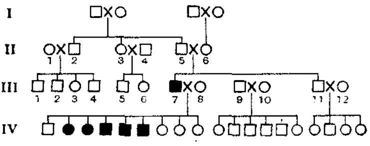


FIG. 46.—HYPERKERATOSIS OF THE NAILS. (After Clemente.)

Hereditary DYSTROPHY OF THE NAILS AND HAIR has been described by several authors. Oliver (1925) gives a brief account of its occurrence in grandmother, daughter and granddaughter. Jacobson's (1928) pedigree (Fig. 47) contains 22 cases in five generations of an American family. He cites four families from the literature showing congenital alopecia and congenital dystrophy of finger and toe nails, and has collected six more pedigrees. The condition is a simple dominant in all pedigrees. The nails show hyperkeratosis as described by Wilson (p. 158) and others, but the skin is also dry and rough, the hair very fine, dry and brittle, sparse, with no eyebrows and few lashes, the rest of the body being devoid of hair, except that 4 of the 22 affected individuals had patches of normal hair on the scalp. In the six pedigrees together 58 ♂♂ and 59 ♀♀ are affected. There is a marked tendency for affected individuals to be less numerous and less extreme in later generations. In some of the pedigrees these conditions are associated with defects of teeth, organs of special sense and the central nervous system, thus indicating a general ectodermal defect.

Thompson (1928) has described dystrophy of the nails

only in another American pedigree, which shows 15 cases (10♂, 5♀) in four generations. The nails on hands and feet appear to grow in thickness rather than length, except at the base. It is a simple dominant, except that in one case it skipped two generations. This also appears to decrease in severity in later generations. Walter and Bradford (1928) describe a pedigree with 27 affected persons in five generations. In 20 the keratosis is limited to the nails of the thumbs and index fingers. It is transmitted principally by females and has increased in severity in successive generations.

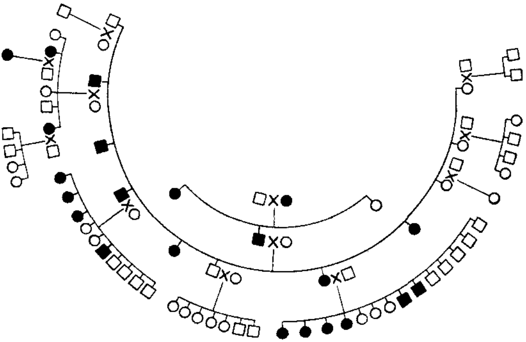


FIG. 47.—DYSTROPHY OF HAIR AND NAILS. (After Jacobson.)

Pires de Lima (1924) describes a family with ONYCHATROPHY, the nails on hands and feet more or less atrophied and deformed. A normal woman had three normal sons and two daughters with onychatrophy. One of these daughters had a normal son and three daughters all with nails more or less atrophied. Hence the condition was confined to the female line for three generations (hologynic).

POLYDACTYLY and SYNDACTYLY (fingers or toes united by a web of flesh) are well known as inherited conditions, and may be considered together. The frequency of syndactyly is probably not more than 1 : 1,000, and of polydactyly slightly higher. Reaumur's case of a Maltese couple having a hexadactylous son, three of whose children were again hexadactylous,

is referred to by Huxley (*Darwiniana*, p. 35). But usually such pedigrees are incomplete, no account being taken of the normal members of the family. Windle (1891) cites an instance from Clement Lucas, where six fingers or toes were inherited in a family through four generations. There appear to have been twenty-five normals to seventeen hexadactyls. In other records the condition has been followed for six and five generations respectively. There is some evidence that polydactyly is more common in negroes than in whites.*

Lewis (1909*b*) describes Lucas's case, in which in several related families in two generations there are twenty-four normals to fifteen polydactyls. Other records cited show that the abnormality may skip a generation. There is a large degree of variation in the extent to which this dominant character is developed. Bonavia (1895) gives several pedigrees of hexadactyly in man, with a good many cases of the inheritance of various abnormalities and sudden monstrous variations in a number of different animals. Polydactylism is found not only in man, horses, fowls, and guinea-pigs, but also in monkeys, dogs, cats, and other animals.

Albert (1915) describes a family with thirteen cases of fused or webbed fingers or toes traced through four generations. The condition was obviously hereditary, but was not inherited as a regular dominant or recessive character. In three cases it appeared in children neither of whose parents were affected, when at least one of the parents had also a normal family history. Probably such irregularities in the expression of a character result from inhibition of its development by the presence of other determiners. Many instances of the influence of hereditary determiners upon each other are now known from experimental breeding.

Schofield (1922) describes a case of webbed toes which occurs in fourteen male members of a family in four generations (Fig. 50). The web appears only between digits II. and III., and is confined to the skin and flesh. It is always more marked in the right foot than the left, and is confined to the males, being transmitted only from father to son. It thus follows the course of the Y-chromosome. The only case of

* That hexadactyly is not modern in origin is shown by the record in the Mitcham Parish Register (quoted in Lyon's *Environs of London*, 1811), vol. i., p. 261, of Anne, the daughter of George Washford, who had twenty-four fingers and toes and was baptised October 19, 1690. I am indebted to Prof. E. Barclay-Smith for this reference.

this type of inheritance which has been experimentally investigated (Schmidt, 1920) occurs in the "millions" fish, *Lebistes reticulatus*, which is a native of the West Indies. A dark spot on the dorsal fin in certain males is transmitted in crosses to all the male offspring, but is not transmitted through the female line at all. Castle (1922) also pointed out the significance of this type of inheritance in man.

He has since (1923) published a Delaware pedigree with 4 cases (all females) of webbed toes in three generations, and suggests that if crossing over can take place between the X- and Y-chromosomes in man, as appears in Lebistes, then the gene for webbed toes may be in the X-chromosome in this pedigree. But if that is the case the inheritance should be not only from mother to daughter (*cf.* Fig. 8, p. 23), but also from mother to son. Castle's pedigree is not extensive enough to show that such transmission does not occur, but four sons who might have had the condition are normal. Castle finds

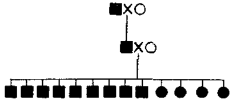


FIG. 48.—PEDIGREE OF SYNDACTYLY. (After Fantham.)

that in all the pedigrees together 65 cases of transmission from parent to child are reported—41 of these are from father to son (holandric), 17 from father to daughter, 3 from mother to son, and 4 from mother to daughter.

A pedigree by Fantham (1924) of syndactyly in a family of Scotch descent in South Africa (Fig. 48) shows the male-to-male descent, but in the third generation the condition was transmitted to all the daughters as well—a circumstance which is difficult to explain unless the father was homozygous. Toes II. and III. were webbed together in all cases, with a peculiar resulting gait. Another pedigree of holandric descent is so striking that it is introduced here (Fig. 49). Fantham (1924) describes the family from the Transvaal. The abnormality occurs only in males, 11 cases occurring in five generations, and the descent is only from father to son, like the Y-chromosome. Unfortunately, the offspring of the women who married were apparently not examined, so it is possible that normal women transmit it to their sons. The account is not quite

clear, but the anomaly occurs apparently in the left hand only. The little finger is flexed so that the first and third phalanges are parallel and practically touching.

Fantham (1925) describes a native family in South Africa in three generations with a supernumerary little toe. The condition was variably dominant, skipping a generation in one case.

O. Thomsen (1927), in a full discussion of polydactyly and syndactyly in man, gives a number of pedigrees, with photographs and radiograms. He discusses Schofield's case of male-to-male inheritance, and gives a similar pedigree with 12 cases in three generations, but two of them are females. He suggests that only one gene is involved in each pedigree, but that this differs in different pedigrees. The effect of the gene is also phenotypically modifiable in varying degrees, and the

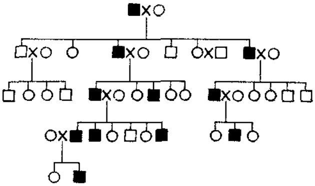


FIG. 49.—PEDIGREE OF BENT LITTLE FINGER. (After Fantham.)

condition may occasionally be almost or entirely suppressed when the gene is present. In some pedigrees women are often carriers, but this will not explain the pedigrees of "Y-chromosome" inheritance. The suggestion is made that in these cases there may be selection of the X-less sperms which bear the specific gene for syndactyly.

Polydactyly and syndactyly in various forms are not infrequently found together. A case of the kind has been described in cats (Howe, 1902). A strain of polydactylous cats in Cambridge, Massachusetts, was descended from a polydactyl cat at the Harvard Astronomical Observatory. One of these cats was dissected, having six toes on each fore paw, and the toes of the hind paws fused in pairs almost to the ends of the claws.

Castle (1906) has described the origin of a polydactylous

race of guinea-pigs. He says that in man "polydactylism usually makes its (recorded) appearance in some noteworthy form, is transmitted more or less strongly through two to five generations, and then disappears, doubtless so weakened by repeated outcrosses that its manifestations, if any occur, are no longer observed." Normal guinea-pigs have four toes on each front foot, but only three on each hind foot. Castle's polydactylous race had four on all feet. The missing digits in normals are the thumb from the fore feet, and I. and V. from the hind feet. The polydactylous race was established from one rare individual (mutation), and was afterwards found twice in breeders' animals, but was not hitherto known in any wild or domesticated *Caviidæ*. By selection through five generations a polydactylous race was gradually established in which all the offspring were polydactylous. The inheritance is neither Mendelian nor blending, but is regarded as probably intermediate between the two. Without the aid of selection, polydactylism would probably never become a racial character.

Stockard (1927) produced by selection a strain of guinea-pigs with five toes on its front feet, which he regards as a reversion to an ancestral condition, the germinal basis for five toes being still present in normal guinea-pigs, but unexpressed, the modern races having four toes on their fore feet and three on their hind feet. Extra toes appeared on the hind feet of a few individuals in eight different stocks. By breeding extra × extra, all the offspring finally had extra toes in various degrees of perfection.

In poultry, Bateson, Davenport, and others have shown that the extra toe, which has for a long time been an established character in some breeds, is not strictly Mendelian in its inheritance, although it is more strongly established than in the four-toed race of guinea-pigs.

Radiograms of a hexadactylous Italian immigrant with six fingers and toes are given in *Journ. Heredity*, vii. 320 (1916). The condition appears to be due to a split in the rudiment of the fifth finger. A five-toed pigeon, due to a similar split in the rudiment of one toe, is also shown. A case in which the thumb is more or less completely missing from both hands is photographed in *Journ. Heredity*, vii. 224 (1916). There were various digital malformations in the relatives.

Bond (1920) crossed various five-toed and four-toed breeds of fowls. The former were the silky Dorking and Faverolle, and the latter Old English Game, Wyandotte, and Orpington.

The proportions of four-toed to five-toed and heterodactylous birds (with four toes on one foot and five on the other) varied somewhat according to whether the male or female belonged to the five-toed breed, and also in F_1 as compared with F_2. In a total of 402 birds, 172 had four toes on both feet, and 38 were heterodactylous. Of the latter, 34 had the extra digit on the left side and only 4 on the right. In 2 birds rudiments of six toes appeared, suggesting that the character for extra toe is not stable. Bateson and Punnett also found that among 89 asymmetric birds from various matings, the extra digit was on the left side in 72 cases, and on the right in 17. In 49 other birds the extra toe was larger on one side than on the other, being larger on the left side in 34 of these cases, and smaller in 15. Barfurth (1911), in similar matings between normal and hyperdactylous fowls, obtained 556 four-toed and 475 hyperdactylous. Of the latter, 65 were asymmetrical, 35 having the extra toe on the left and 30 on the right. In another list 12 birds were left-sided and 6 right-sided.

In further observations on this subject, Bond (1926) found that in crosses between Houdan (five-toed) and Andalusian (four-toed), the F_1 shows a preponderance of five-toed, a few birds being asymmetrical, with the extra toe more often on the left side. There were also 3 birds with six toes on one foot and five on the other, and 1 bird had six toes on both feet. The F_2 contained 26 with five toes, 14 with four toes, and 6 asymmetrical. It appears that the genetic factor controlling the extra toe may influence any of the toes and may even cause an extra metatarsal bone. Castle (1906) in guinea-pigs also found a slight tendency for the extra toe to appear on the left side. Out of 1,219 individuals, 630 had the extra digit on the left and 582 on the right. The explanation is not clear.

Barfurth (1911) noticed that in eight-day chicks with an extra toe, an extra rudimentary digit also appeared on the wing. Occasionally the latter appears without the former. Hence both limbs are affected in fowls, as in man and the guinea-pig. Danforth (1919*a*) suggested that syndactyly in fowls, like brachydactyly, is another form of expression of the factor for leg-feathering.

Bonnevie (1919) describes a type of postaxial polydactyly in man, which is usually stronger on the right side of the body. The extra finger arises from the base of the little finger, the metacarpal bones being normal. There is much variation in this abnormality, and families showing it are now distributed all

over Norway, but they are all probably descended from the same ancestor about 300 years ago.

Sverdrup (1922) has carefully analysed a Norwegian family with dominant polydactylism in six generations beginning with a woman living about 1800. The abnormality consists in an additional digit on the postaxial, ulnar, or outer side—*i.e.*, a little finger or a portion of one. This is associated with brachydactylism, apparently due to shortening of the metacarpals and metatarsals. Sometimes it occurs in one hand and both feet, or it may be in one hand and one foot, or only in the hands. The extra digit varies from a wart-like appendage to a complete finger or toe with metacarpal phalanges and nail. Two types of the condition are recognised, with intergradations. A consists in the duplication of a digit, usually V. In the B type a small appendage is loosely attached to the ulnar border of the hand, and there is no shortening of the metacarpals, but people with B type hands have A type feet. A type parents can have B type children, but B type parents cannot have A type children. All the polydactyls are heterozygous, and 12 families from DR × RR matings produced 34 polydactyl : 23 normal siblings. One line of descent belongs mostly to the A type, another entirely to the B. The B type is produced by a single factor, and the A type is probably due to an additional modifying factor. Koehler (1924) gives fourteen pedigrees of polydactyly, and he also distinguishes between a complete extra finger or toe and a small extra portion, but the genetic results of his work are not very clear.

Boas (1917) assigns two causes for polydactyly in horses: (1) Atavism, "*Hipparion*-toes"; (2) doubling of certain digital parts of the foot. The case of Cæsar's horse, which belonged to the former class, is well known.* This condition is rare. Dechambre (1922) describes an extra digit on the right fore foot of a horse, and cites 25 cases of polydactyly in the horse, from the literature since 1853. More or less complete doubling of the extremities occurs in various mammals. Cramer (1910) discusses cases of polydactyly in man, horses, a lamb, fowls,

* The reference is in Suetonius, Bk. I., chap. lxi.: "Utebatur autem equo insigni, pedibus prope humanis et in modum digitorum ungulis fissis." ("He rode a remarkable horse too, with feet that were almost human, for its hoofs were cloven in such a way as to look like toes.") The writer goes on to say that it was born in Cæsar's stables, that he tended it with great care and was the first to mount it, and that a statue of it was afterwards dedicated in front of the temple of Venus Genetrix.

pigs, and a calf. Fackenheim (1888) describes a family in which hereditary polydactyly is combined with tooth anomalies. The Heizler family showed polydactyly as a simple dominant in four generations. A polydactylous man of the third generation married a woman with tooth anomalies, having two abnormally large, pointed teeth in place of the incisors and only two cheek teeth. Of their six children, three were normal and three showed both abnormalities with some variations in the condition of the teeth.

A recent case of polydactylism in cattle is described (Roberts, 1921). Many instances have been recorded. In this one, from a herd of dairy cattle in Illinois, a normal bull mated with a polydactylous cow, having three toes on each foot, produced a polydactylous female. She was mated to a normal unrelated bull and produced three male calves, all polydactylous, but one with a duplication of the metatarsal bones of the hind feet, which bore four and five toes respectively. The character is evidently dominant in inheritance. The third or extra toe is on the inside, and probably represents digit II. It is always larger on the hind feet than on the fore feet.

Bateson (1894, p. 376) describes a three-toed strain of cattle from a three-toed cow bought in 1861. The strain lasted until 1887, producing about ten generations. The condition appeared in both males and females, but the bulls were not kept, so transmission was only through the cows. About two calves in three had the extra toe. The abnormality was confined to the hind feet, except in one case. As the last members of the strain were all males the breed was lost. This instance of polydactyly is very similar to the last. The inheritance was evidently the same, but the character itself shows the interesting difference that it is less extreme. It is confined to the hind feet, except in one individual, whereas in Roberts's herd it is present on all four feet, but is larger on the hind feet. Such slight constant differences in abnormalities are of fairly frequent occurrence, and they throw an interesting sidelight on the structure of the germ plasm and the almost infinite variety of the changes which it can undergo.

A very good case of syndactyly in ungulates is that of the mule-foot hog, a type with solid instead of cloven hoofs, which has long been known in the Western States of America, and is also found in Germany and elsewhere. Detlefsen and Carmichael (1921) find that in crosses between a pure-bred mule, foot boar and pure-bred Duroc-Jersey sows the offspring-

numbering about 250, were all black and mule-footed like the sire. Later generations showed that syndactyly was a simple dominant to normal, and black to red of various shades.

Bateson (p. 387) gives numerous data on the subject. He states that solid hoofs in pigs is a relatively common variation, that they are mentioned by Aristotle, and are found in various parts of the world. Sir N. Menzies, at Rannock, Scotland, had a breed of such hogs for forty years. They came from a pair, and were black and of smaller size than the type, with smaller ears. Their flesh was considered more sweet and tender, and several hundred were bred at a time. In crosses they showed alternative inheritance, but they finally became extinct. Another pair of solid-hoofed pigs was received by the Zoological Society of London from Cuba in 1876. Auld (1889) reports soliped (solid-hooved) swine from Texas in 1878. They bred true, and when crossed with the normal gave a majority of solipeds. Another breed of solid-hoofed hogs was reported from a farm at Sioux City, Iowa, and a wild herd from near Baton Rouge, Louisiana. In another instance a Poland-China boar with *one* solid hoof had many offspring in the same condition. Probably the solid-hoofed condition has arisen many times through independent mutations.

A peculiar case is recorded by Colonel Hallam* of a race of pigs observed in a town on the coast of the Tanjore country in 1795. Drawings of two individuals were submitted. The pigs had only two legs, the hinder extremities being entirely wanting. They bred true for at least three generations. Such cases must arise through some mishap to an element of the germ plasm.

Darwin† cites the following conditions in horses as plainly hereditary: ring-bones, curbs, splints, spavins, founder and weakness of the front legs, roaring or broken and thick wind, melanosis, specific ophthalmia, blindness, crib-biting, jibbing, and ill-temper. He quotes Youatt: "There is scarcely a malady to which the horse is subject which is not hereditary."

Many records of syndactyly in man are extant, but usually the inheritance has only been traced from parent to offspring. It is recognised as a Mendelian dominant condition. Hurlin (1921) describes a case of limited syndactyly in an old New England family in which the web occurs only between the

* *Proc. Zool. Soc.*, 1833, Part I., p. 16.

† *Animals and Plants*, chap. xii., p. 454.

second and third toes, and is sometimes even there so slight as to be scarcely noticeable. It is not found in the hands at all. The condition is found in the grandfather, in his only child (a son), and in three out of six of the F_2 generation in accordance with Mendelian expectation. There is no doubt that innumerable slight abnormalities of this kind occur in man and are inherited in the Mendelian manner, as has been shown to be the case with many similar mutations in *Drosophila*.

Schultz (1922) adopts Weidenreich's term zygodactyly for true webbing, confining the term syndactyly to those cases where a union or fusion of bones is involved. Zygodactyly is found in many mammals. In a Sumatran ape *Siamanga syndactyla* (see Wallace, *Malay Archipelago*, p. 134), the two first digits of the feet are joined together nearly to the end. Webbing also occurs in the related Hylobates. In an early stage of development of the human foot the toes are all webbed, and the webbing extends slightly further between the second and third toes than between any others. Webbing or zygodactyly is, therefore, a case of arrested development. It is also found that when certain toes are webbed the corresponding tendons are joined for a greater distance. Schultz cites the observations of Schurmeier, who examined 20,000 men in the American army and found 8 cases of zygodactyly, always between toes II. and III. This condition was combined in some cases with webbing of fingers III. and IV., or I. and II. and III. and IV., or all fingers. In a family described by Sommer, the webbing of toes II. and III. was only on the right foot in all members, the pedigree extending through five generations. It was inherited by both sexes, probably as a simple dominant. In Schofield's (1922) family (Fig. 50) the webbing is always longer on the right foot and is transmitted only from male to male, appearing in all the sons (13 cases) and none of the daughters (11 cases) and following the Y-chromosome. In Hurlin's family, mentioned above, the webbing was longer on the left foot and was exhibited in both sexes. In three other families, by Pfitzner, Wolff, and Wile, the character also appears to be a simple dominant.

Syndactyly and polydactyly appear together in the family described by Manson (1915, 1928). This family (Fig. 51) originated from one William Joseph, born in Aberystwyth about the beginning of the nineteenth century. He had webbing of the third and fourth fingers of both hands, and six toes on each foot, and was probably homozygous for this

condition, since his nine children all had it. Three of them married normals, and had a total of nineteen descendants affected, with twenty-two normal sibs. In only three descend-

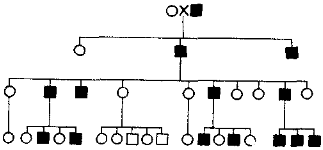


FIG. 50.—INHERITANCE OF WEBBED TOES. (After Schofield.)

ants is the abnormality complete in all four limbs. One, two, or three limbs may escape. Skiagraphs show incomplete polydactylism in some cases. There is considerable variation

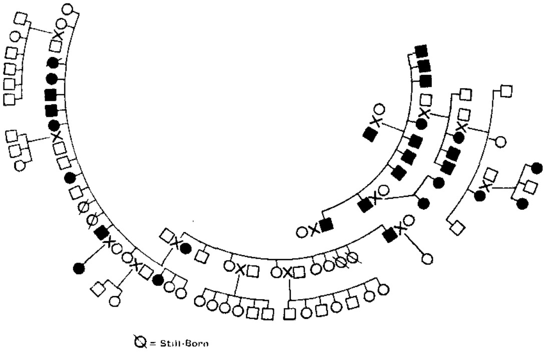


FIG. 51.—HEREDITARY SYNDACTYLY AND POLYDACTYLY. (After Manson.)

in the condition, but skiagraphs show clearly that the fourth digit of the hands and feet is consistently affected by complete or partial reduplication.

Polydactyly in the feet is apparently due to an extra digit interpolated between digits IV. and V. The more complete

the polydactyly, the greater is the tendency to syndactyly. Hence these are regarded not as separate characters but as expressions of one factor. The presence of extra sesamoid bones in these hands (as is frequent in embryo hands) indicates that the processes of absorption are below normal. Since the webbing also indicates a failure of absorption, syndactyly, and even in some sense polydactyly, may be regarded as a failure to complete development. Another polydactylous family is described by Atwood and Pond (1917).

Many data concerning hyperdactyly are given in a paper by Ballowitz (1904), who gives several pedigrees of dominant polydactyly, but without mentioning the Mendelian explanation. Records of extra fingers and toes are known not only in Caucasians, but also in negroes, Arabs, Chinese, and Amerinds (North American Indians). Most frequently only an extra terminal phalanx is present, but six-fingered men have been known from the earliest times. In the Bible (2 Sam. xxi. 20) a " giant " is mentioned who had six fingers on each hand and six toes on each foot. He was one of four men of exceptional stature—sons of a giant. Pliny referred to hexadactylous persons as Sedigiti. Anne Boleyn, the beautiful wife of Henry VIII., is said to have had supernumerary breasts,* teeth anomalies, and an extra terminal phalanx on hands and feet.† The " outside " digits—*i.e.*, thumb and little finger and great and little toe—most commonly show doubling. Doubling of other digits is much more uncommon, becoming still more so as the number increases. Thus the presence of ten digits on one hand or foot is extremely uncommon in museums, while cases of seven are relatively often described. This condition is often combined with other abnormalities, but hexadactyly and heptadactyly often occur in otherwise normal individuals. The extra digits are frequently syndactylous, not fully separated from their neighbours. Hexadactyly is often symmetrical (two

* Other cases of supernumerary mammæ (polymastia) in more than one generation are cited, for example, by Darwin, *Descent of Man*, p. 41.

† The only confirmation of this statement I have been able to find is the following, from Wyat's *Life of Anne Boleyn* (ed. Singer, p. 423) : " There was found, indeed, upon the side of her nail upon one of her fingers some little show of a nail, which yet was so small, by the report of those that have seen her, as the work-master seemed to leave it an occasion of greater grace to her hand, which, with the tip of one of her other fingers, might be, and usually was, by her hidden, without any least blemish to it." It is a fact, however, that among the portraits of the wives of Henry VIII., Anne Boleyn's is the only one in which the hands are not shown.

double thumbs or two double little fingers), but there are many exceptions, and scarcely two cases agree in detail.

Three main types of abnormality appear: (1) Simplest and most common; the extra digit is a small attachment not adherent to the skeleton, and often without bones or cartilage, muscle or tendons. (2) Often the extra digit is more or less like an ordinary finger or toe, containing bones and connected with the skeleton of the finger. (3) Very seldom the extra digit is complete and also has its own metacarpal or metatarsal bone. All possible intergrades occur between these forms.

Russian statistics are quoted of fourteen families in which the extra finger is inherited, also ten families with six fingers and six toes, while Hennig in 1880 recorded polydactyly in seventy-seven families. The condition may extend through two to five or many generations, and ten to forty hyperdactylous individuals have been recorded in many families. Polydactylous twins are twice recorded, and one polydactylous twin sister had four normal sisters. Reaumur's Maltese family is also quoted in detail by Ballowitz. In two generations descended from Gratio Kaleïa, who had six fingers on each hand and six toes on each foot, and his normal wife, there were ten hexadactyls and six normals, but in the former the abnormality did not always appear on all four limbs. In the pedigree of Elizabeth Horstmann, of Rostock (Mecklenburg), who had six digits on all four limbs, her daughter was like the mother, and the next two generations from marriages with normals gave seven hexadactyl to seven normal, in conformity with expectation for a simple Mendelian dominant. In another pedigree, Marie Schweizer, of Fischbach, three generations of descendants include eight hexadactyl and ten normal. In yet another hexadactylous pedigree (Alexander) there were in three generations of descendants nine hexadactyls to ten normals. All hexadactylous individuals in this pedigree showed a striking symmetry, and in one male the condition was combined with syndactyly.

In another pedigree, quoted from Marchand, in which the condition ran through five generations, a family of eight in the fourth generation all had six fingers and six toes. The father, who was hexadactylous, must have been homozygous for the trait. The family of the Sultan of Pontianak (Borneo) is hexadactylous, and this condition is recognised in each generation as a mark of royal distinction! Ballowitz quotes from the French literature (1863) the case of an isolated

village in the Département d'Isère, in which, through inbreeding, nearly all the inhabitants had six fingers and toes. Later, owing to increased communications, marriages with normals took place, and the extra fingers and toes in newborn children became smaller and fewer, finally disappearing altogether. This is a good example of the " weakening " and disappearance of an abnormality through exogamy, but brachydactyly does not appear to be affected in this way. If such weakening of a character like hexadactyly can take place through exogamy, it is an important hereditary principle which requires further elucidation, especially in comparison with conditions like brachydactyly where no weakening effect is observed even after many generations of outcrossing.

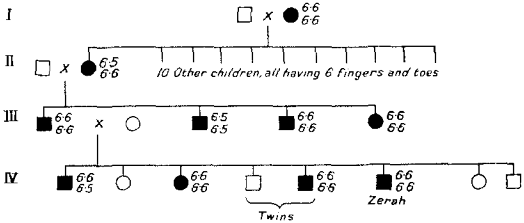


FIG. 52.—PEDIGREE OF HEXADACTYLY. (After Carlisle.)

An interesting hexadactylous family is described by Carlisle (1814). Zerah Colburn, the son of Abiah Colburn, born in Vermont, was brought to London on account of his " extraordinary powers in arithmetical computations from memory." He had a supernumerary little finger on each hand, and an extra little toe on each foot. The extra digits were all perfectly formed, with nails and three phalanges. The father also was hexadactylous, having five metacarpal bones, but six metatarsals. The pedigree of this family through four generations is given in Fig. 52. Beside each is given (above) the number of fingers and (below) the number of toes. The inheritance is strictly that of a Mendelian dominant, with occasional failure of one hand or foot to exhibit the abnormality.

In another hexadactylous family (Sedgwick, 1863, p. 188) an extra finger with two phalanges and a nail was attached to the base of the first phalanx of each little finger. The condition

was followed through four generations. There was some variation in its expression, and it skipped two generations both in the male and the female line (see Fig. 53).

Straus (1926) has made a recent survey of zygodactyly in man and animals, with five new pedigrees in man. The condition appears in kangaroos, rodents, and insectivores, and is, of course, also associated with aquatic habits. Considering the eleven known pedigrees in man, Straus finds that in the majority zygodactyly is a simple dominant, in two others it is either dominant or sex-linked, while in three cases it appears as a recessive or else it arose as a mutation. In one it follows the Y-chromosome. In one pair of apparently identical twins

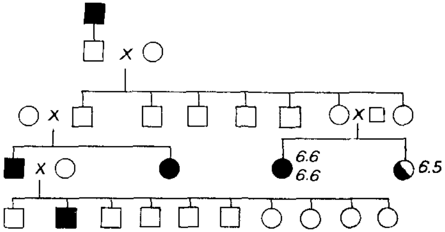


FIG. 53.—HEXADACTYLOUS FAMILY. (After Sedgwick.)

only one has webbing. Wölfflin (1926) presents a pedigree of webbing which is found alternatively in males and females of successive generations. Whether this has any special significance is as yet uncertain.

Staff (1926) has a pedigree of syndactyly and polydactyly in six generations. Both sexes are equally affected. He discusses the time-worn hypothesis of amniotic folding and pressure as a cause, but finally concludes that a germinal variation was probably involved.

LeGros Clark (1916) describes a syndactylous family of another kind. Both hands of a girl of twenty were lacking digits I., II. and III., and digits IV. and V. were fused. Metacarpals IV. and V. were normal, but a metacarpal bone was lying crosswise between the heads of metacarpals III. and IV. The father and two brothers of this girl had the same abnormality—hypodactyly combined with syndactyly.

Schroeder (1918) described a condition of HYPODACTYLY

appearing in the hands and feet of a family for five generations and accompanied by other deformities. The strain originated with a woman, who is said to have had normal parents. She produced three affected and two normal children, the latter having only normal descendants, while the former had twenty-eight normals to sixteen affected offspring. The condition is transmitted by both sexes, and shows a tendency to become less marked in later generations.

Hawkes (1914) has compared different types of human foot as regards the relative lengths of the first and second digits. From an examination of the feet of 2,300 persons, chiefly children, he finds the " L " type of foot, with the great toe longest and the other toes sloping back in an oblique line, the commonest. The " S " type, in which the second toe is longer than the great toe, is much less common. Not very rarely one foot will be of the L type, and one of the S type. This is in heterozygotes, but some persons with both feet L are heterozygous. The " E " type, in which digits I. and II. are of equal length, is very unusual. The L type of foot shows irregular dominance over the S type in inheritance, but the S type occurs more commonly in females than in males, and is commonest in the fœtal stage. The male heterozygote tends to be L, and the female to be S, in foot pattern. Occasionally digit III. is longer than digit II., and this condition is also found to be hereditary.

Manson (1928) describes a man (H. F.) with the fingers of both hands deviated towards the ulnar side (clinodactyly), hollowing of the palms, and a very prominent first carpo-metacarpal joint. His feet were similar. He inherited the condition from his mother, who showed the condition in her feet but had normal hands. A sister of H. F. was like the mother, while two brothers were normal. H. F. had a son who was normal, a daughter with high plantar arches but normal hands, and a younger son with plantar arches in both feet.

A striking pedigree, because it is one of the first showing genetic linkage between dissimilar traits, is that of Tomesku (1928) in Fig. 54. In affected members of this family the little finger is crooked, the terminal phalanx being bent inwards (to the radial side), digits II. and IV. being similarly affected to a less extent. A slightly bent little finger is probably not uncommon as an inherited trait. The above pedigree contains 16 cases, and all were brunettes with black hair. Those with

blond or brown hair did not have clinodactyly. The two dominants appear to be closely linked. Tomesku cites Weber (without giving the reference) as observing that in a family the members with red hair had exostoses, while the brunettes were free from this deformation. Exceptions or cross-overs would add still further to the interest of such pedigrees.

Ellsworth (1927) describes the inheritance of a condition in which the carpus is displaced forwards on the radius and ulna, and the wrist articulations are deformed. From a small pedigree in which five females in four generations show the condition, it appears that it may be a simple dominant not sex-linked.

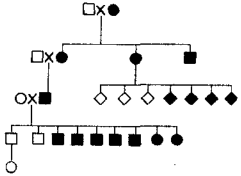


FIG. 54.—PEDIGREE OF CLINODACTYLY AND BRUNETTE COMPLEXION. (After Tomesku.)

LUXATIO COXÆ, or congenital dislocation of the hip, has been recently studied from an inheritance point of view. Roch (1925) was the first to collect a large material on its inheritance from the clinics of Tübingen and Leipzig. He cites 189 cases in 29 pedigrees. The condition has been considered in medical literature from the time of Hippocrates. Roch finds it 5·5 times as frequent in women as men. It is usually recessive, but in certain families appears to be dominant. He regards it as a sign of degeneration, more frequent in families whose ancestors contained drinkers and epileptics. Bryn (1926) finds that the condition is very frequent in the hybrid population of Finmark, compared with other parts of Scandinavia. It has been repeatedly shown to be very much more frequent in hybrid than in pure races. In Lapp × Norwegian, the small pelvis and narrow acetabulum of the Lapp woman, combined with the large caput femoris of the Norwegian, makes luxation easy, and may be regarded as a disharmony arising from this cross. Hooff (1928) has found 932 cases (132 ♂, 800 ♀,) among 14,320 examined in ten years at the orthopædic hospital

in Munich. It was thus six times as frequent in females as in males, and 20 per cent. of the cases were familial. It appears in some pedigrees like an irregular dominant, but Hooff concludes that the co-operation of several genetic factors may be necessary to produce the condition, one or more of them being dominant. In a pair of twins very probably identical, only one of them had it. The greater frequency of luxation in female children is due to the difference in shape of the pelvis, although in newborn children there is a difference of less than 1 degree in the angle the femur makes with the horizontal in the two sexes. But during the first year the differences increase. Luxation is significantly more frequent in the left than the right femur, especially in the female sex, but there is no known reason why this should be so. Frequently (in 42 per cent. of cases)

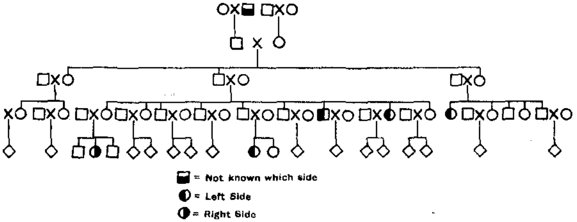


FIG. 55.—INHERITANCE OF LUXATIO COXÆ. (After Hooff.)

both femurs are dislocated. Hayashi and Matsuoka found luxation relatively common in Tokyo. This is ascribed to the fact that the Japanese are compounded of Mongolian, Ainu, and Polynesian elements. Luxation is also known to occur in North Africa, Sudan, Madagascar, and Annam; whereas among the Chinese of Shanghai, who are regarded as a pure race, it is said to be almost non-existent, only three cases occurring in twenty years in a hospital clinic seeing 70,000 patients annually. There are also great differences in its frequency in parts of Germany and the Tyrol. Hooff produces 112 pedigrees, a characteristic one of which is reproduced here (Fig. 55).

In his breeding experiments with mice, Rabaud (1919) describes the appearance of a race from wild × albino, in which

the tibia is replaced more or less completely by a fibrous tract, while the fibula is heavy and incurved. As a result, the leg is bent on the thigh and will not support the animal. It walks on the distal end of the femur, which thus appears dislocated. This condition only appeared in the descendants of one pair from the original cross. When crossed with normal it was recessive, usually giving a 3 : 1 ratio. Two abnormals crossed together afterwards gave 18 normal : 74 abnormal, 9 of them "luxated" on one side only. Extracted normals crossed together gave 3 : 1, and normal × "luxated" gave 1 : 1. These inheritance results show some similarity to those described above for luxatio coxæ in man.

Extreme HYPERMOBILITY, or a "double-jointed" condition, is described (Key, 1927) in a father and four sons, but not in the five daughters. One would like to know more before concluding about the method of inheritance, but this may be another case of male-to-male (holandric) inheritance.

Terry and Cady (1923), in a discussion of the question whether the SUPRACONDYLOID PROCESS is really more frequent in the insane, after quoting various statistics showing its incidence in St. Petersburg, Italy, and France, found that in St. Louis, Missouri, 7 among 1,000 of the poorer class had the process. Among 1,000 mental defectives in the same city 12 had it, suggesting a slightly higher incidence in the insane. A MALFORMATION OF THE ELBOW JOINT is described by Herzog (1927) in a woman, her sister, father, and grandmother. It was bilateral in all and consisted in the separation of the broad fossa olecrani into a lateral and a deep medial recess, the olecranon small and slightly arched. X-ray examination showed that the mechanism of movement was also abnormal. The inheritance suggests a simple dominant.

ACHEIROPODIA, or absence of hands and feet, is described in a family from Brazil (Peacock, 1929). This condition is rarely observed and shows different aspects in different pedigrees. The condition was dominant in this family, the father and his brother being abnormal, and the three children all like their father. Only stumps of the arms and legs are present; the long bones of the legs develop, but the muscles are absent. The deformed arms develop a nail at the tip. Rudimentary development of the distal end of the limb bud is the essential condition. Three other pedigrees of this appalling abnormality are cited.

Danforth (1924) records in twenty dissected cadavers the

deviations from normal in the anatomical structure of the arms and legs. Notes were kept of 157 pairs of structures (muscles, bloodvessels, and nerves) in each. The departures from normal amounted to 7 to 9 per cent., mostly bilateral, but some unilateral. There is evidence that both are germinal in origin, and there is no evidence that the unilateral differs genetically from the bilateral. Most of the traits appearing are probably best considered as due to modifying factors. The gene for each abnormality has its peculiar potency, usually admitting of certain failures to appear. The sides of the body and the sex of the individual act as influences definitely favouring or inhibiting the appearance of various traits represented in the germ plasm.

Left-handedness.

This is an innocuous feature, the inheritance of which is generally recognised, but the manner of its inheritance is still uncertain. The results of Jordan (1911) and of Hurst (1912) were regarded as indicating that it is a simple Mendelian recessive character, at least in some families. Ramaley (1913) came to the same conclusion, based on 1,740 cases. He estimated that the condition is carried in about one-sixth of the population. Left-handedness, as a character, may bear some resemblance to reversed symmetry in certain Gastropods. This reversal has been shown by Conklin to begin in development with the cleavage of the egg, the spiral cleavage being dextral in one case and sinistral in the other, but the inheritance of this difference is also complicated, as shown by the work of Diver, Boycott, and others, and it is not yet understood.

Ambidextrous individuals in man appear to have inherited left-handedness and acquired dexterity with the right hand. There are apparent exceptions, however (see Compton, 1912), as in a family quoted by D. J. Cunningham in the *Journal of the Anthropological Institute*, xxxii., 1902, from Aimé Péré, where a left-handed mother and a right-handed father had eight sons and six daughters, all left-handed. If the father were heterozygous, this result would be possible, though very improbable, even if left-handedness were regarded as a recessive. It would seem more probable that in such a case the dominance has been reversed. Such reversal of dominance is now known in many human pedigrees. There is also clear evidence that in certain families the condition is sex-linked.

A paper by Beeley (1920) considers left-handedness from

various points of view, and gives a number of references to the literature of the subject. Estimates of the frequency of left-handedness have varied between 6 and 2 per cent., with 4 per cent. as the medium frequency. This applies to American Indians (Apaches and Pimas), as well as to white races. That the condition is more frequent in man than in woman has been affirmed and denied. Some have found it more frequent among delinquents and among negroes, but there seems to be no sufficient basis for these conclusions. Jordan, from an examination of 700 university students, 1,394 coloured school children, and 668 others, concludes that the condition is inherited, but is not very clear that it follows Mendelian principles. Baldwin found that the tendency to use one hand more than the other developed about the seventh month after birth, when all influences to the greater use of one hand were eliminated. The old idea that right-handedness was developed because warriors held the shield with their left hand to protect their heart and wielded the spear with their right will not bear analysis with modern conceptions. That right- or left-handedness does not depend on a difference in the eyes is also shown by the fact that there is the same proportion of left-handed among the congenitally blind as among those who use their eyes.

Beeley considers the results from 106,356 children examined, and concludes that all degrees exist from extreme left-handedness to extreme right-handedness. Among this number of children were found forty-two "mirror-writers." The results showed that mirror-writing is not necessarily correlated with mental deficiency, but rather it is characteristic of extreme left-handedness. A method was devised for measuring the degree of left-handedness by means of a brass plate divided into squares, on which two straight lines at right angles to each other were to be traced. The squares were alternately insulated in such a way that every error produced an electric current which was recorded in a counter. The number of errors in tracing the two lines, multiplied by the time taken, was used as a measure of the degree of left-handedness. Obviously general dexterity would play an important part in a result of this kind, and the age of the child would be an important element in such a result. It is not, therefore, clear that the degree of left-handedness forms such a continuous series as these results would indicate, although it is highly probable, if not certain, that degrees of left-handedness exist. Beeley

suggests that a slightly left-handed child should be taught to use its right, but that an extreme left-hander should not.

That the right hemisphere of the brain controls the left side of the body and *vice versa* is, of course, well known; also that the development of the speech-centre may be interfered with by a too early attempt to teach a left-handed child to use its right hand, thus leading to stuttering.

More recently another unsuccessful attempt has been made to determine the manner of inheritance of left-handedness, but it has added something to our knowledge of the subject. Chamberlain (1928) has again tried to interpret the subject in Mendelian terms. Adopting the questionnaire method, he obtained information from left-handed individuals all over the United States. Many degrees of left-handedness were found and finally writing with the left hand was adopted as an artificial criterion of left-handedness. There are, however, certainly many naturally left-handed people who do not write with the left hand. Then a study was made of 2,177 freshmen in Ohio State University. These with their parents and sibs gave a population of 12,068, of which 4·3 per cent. were left-handed. Of the freshmen themselves, 4·3 per cent. were left-handed. These figures are in accord with earlier records of Lombroso and others for different populations.

Statistics brought out the fact that left-handedness was consistently more frequent in males than females. Thus the fathers in the above families were 4·13 per cent. left-handed, the mothers 2·94 per cent., brothers 6·05 per cent. and sisters 3·76 per cent. Of the males as a whole, 4·96 per cent. were left-handed, and of the females 3·39 per cent.; hence nearly 50 per cent. more males than females. Among 33 families (from two sources) in which both parents were left-handed, 46 per cent. of the children were so. In 55 families where the mother was left-handed 13·77 per cent. of the children were the same; and in 82 families in which the father was left-handed, 9·7 per cent. of the children were. There is evidently some sex-linkage, since mothers transmit the condition more than fathers. But to solve the details of inheritance where at least two factors, one of them sex-linked, are involved, will require the collection and analysis of pedigrees through several generations, in which the collaterals are also included.

The manner of clasping the hands, whether right-handed or left-handed—*i.e.*, with the right thumb over the left or *vice versa*—although characteristic enough for the individual,

apparently bears little relation to right- or left-handedness. It does not follow any known rule of inheritance, but appears, nevertheless, to be partially inherited, for when both parents show a right- or left-handed clasp the majority of the children will be of the same type. Statistics show that *en masse* the two methods usually occur with equal frequency, but neither condition breeds true.

To a few individuals it is immaterial which thumb is on top. Downey (1926) has collected certain data which bear on the question whether the marked tendency to place one thumb uppermost is inherited. Of course it is possible that the tendency to place a particular thumb on top is an early-formed habit. Downey reports on 1,040 ♂ and 541 ♀. He found that 49 per cent. of the men and 54·2 per cent. of the women place the right thumb outside. There is a certain tendency (not very strong) for left-handed people to place the left thumb uppermost in clasping the hands.

Compton (1912) has studied the right and left-handed seedlings (as regards the manner of folding of the first leaf), which occur in various cereals, but the condition is not inherited. Thus the seeds from a left-handed (LH) plant produce the same ratio of LH and RH plants as do the seeds of a right-handed (RH) plant. In two-rowed barley this ratio LH/RH was shown to be constant for three generations, and therefore inherited. In a total of 19,165 seedlings, the percentage of LH seedlings =58·362. Seeds planted from the odd and even rows separately also gave the same preponderance of left-handed plants. Six-rowed barley gave a similar excess of LH plants. In oats, however, there is regularly an excess of RH plants (LH=44·88 per cent.). This difference may have some connection with the fact that the leaf-blades of barley "are generally slightly twisted into a right-handed screw, while in oats the torsion is in the reverse direction." In maize, again, there is no inheritance of left-handedness or right-handedness as such, but the seeds in odd rows give an excess of RH, those from even rows an equal excess of LH seedlings. The ratios were 54·22 per cent., and 46·16 per cent. LH respectively. Thus, the total numbers of LH and RH seedlings from a cob are practically equal. Compton suggests that the differences between rows in this regard may perhaps be accounted for by unequal pressure on the embryos.

LITERATURE

ALBERT, HENRY. 1915. The inheritance of syndactylism. *Science*, xli. 951.

ATWOOD, EDITH S., and POND, CLARA P. 1917. A polydactylous family. *Journ. Hered.*, viii. 96, fig. 1.

AULD, R. C. 1889. Some cases of solid-hoofed hogs and two-toed horses. *Amer. Nat.*, xxiii. 447-449, fig. 1.

BALLOWTIZ, E. 1904. Über hyperdaktyle Familien und die Vererbung der Vielfingerigkeit des Menschen. *Arch. f. Rass. u. Gesells. Biol.*, i. 347-365, figs. 11.

BARFURTH, D. 1911. Der Flügelhöcker des Hühnchens, eine rudimentäre Hyperdactylie. *Arch. f. Entwick.-Mech.*, xxxiii. 255-273, pl. 1, figs. 2.

BATESON, W. 1894. Materials for the Study of Variation. London: Macmillan, pp. 598, figs. 209.

BEELEY, A. L. 1920. Left-Handedness. *Amer. Journ. Phys. Anthrop.*, ii. 389-400.

BOAS, J. E. V. 1917. Zur Beurteilung der Polydaktylie des Pferdes. *Zool. Jahrb. (Anat.)*, xl. 49-104, pl. 1, figs. 51.

BONAVIA, E. 1895. Studies in the evolution of animals. London: Constable, pp. 362, figs. 128.

BOND, C. J. 1920. On the left-sided incidence of the supernumerary digit in heterodactylous fowls. *Journ. Genetics*, x. 87-91.

BOND, C. J. 1926. Further observations on polydactyly and heterodactyly in fowls. *Journ. Genetics*, xvi. 253-256, pls. 2.

BONNEVIE, K. 1919. Polydaktyli i norske bygdeslegter. *Norsk Mag. f. Lägev.*, No. 6, pp. 32.

BREITENBECHER, J. K. 1923. Hereditary shortness of thumbs. *Journ. Hered.*, xiv. 15-22, figs. 11.

BRYN, H. 1926.

CARLISLE, ANTHONY. 1814. An account of a family having hands and feet with supernumerary fingers and toes. *Phil. Trans.*, civ. 94-101.

CASTLE, W. E. 1906. The origin of a polydactylous race of guinea-pigs. *Carnegie Inst. Publ.*, No. 49, 17-29.

CASTLE, W. E. 1922. The Y-chromosome type of sex-linked inheritance in man. *Science*, lv. 703-704.

CASTLE, W. E. 1923. Further data on webbed toes. *Journ. Hered.*, xiv. 209-210, fig. 1.

CHAMBERLAIN, H. D. 1928. The inheritance of left-handedness. *Journ. Hered.*, xix. 557-559.

CHILTON, N. 1927. Hereditary deformity of the fingers. *Brit. Med. Journ.*, ii. 15.

CLARK, W. E. LE GROS. 1916. A case of hereditary syndactyly. *Lancet*, ii. 434, fig. 1.

CLEMENTE, L. S. 1928. A claw-fingered family. *Journ. Hered.*, xix. 529-536, figs. 5.

COMPTON, R. H. 1912. A further contribution to the study of right- and left-handedness. *Journ. Genetics*, ii. 53-70.

CRAGG, E., and DRINKWATER, H. 1916. Hereditary absence of phalanges through five generations. *Journ. Genetics*, vi. 81-89, pl. 1.

CRAMER, M. 1910. Beiträge zur Kenntnis der Polydaktylie und Syndaktylie beim Menschen und einigen Haustieren. *Nov. Acta Abh. k. Leop.-Carol. Deut. Akad. Naturf.*, xciii. 1-40, pls. 6.

CUSHING, HARVEY. 1916. Hereditary ankylosis of the proximal phalangeal joints (Symphalangism). *Genetics*, i. 90-106, figs. 11.

DANFORTH, C. H. 1919*a*. The developmental relations of brachydactyly in the domestic fowl. *Amer. Journ. Anat.*, xxv. 97-115, figs. 5.

DANFORTH, C. H. 1919*b*. Evidence that germ cells are subject to selection on the basis of their genetic potentialities. *Journ. Exptl. Zool.*, xxviii. 385-412.

DANFORTH, C. H. 1924. The heredity of unilateral variations in man. *Genetics*, ix. 199-211.

DECHAMBRE, E. 1922. La polydactylie chez le cheval. *Rev. Zootech.* Paris; xv. 518-522.

DETLEFSON, J. A., and CARMICHAEL, W. J. 1921. Inheritance of syndactylism, black, and dilution in swine. *Journ. Agric. Research*, xx. 595-604, pl. 1.

DOWNEY, J. E. 1926. Further observations on the manner of clasping the hands. *Amer. Nat.*, lx. 387-391.

DRINKWATER, H. 1908. An account of a brachydactylous family. *Proc. Roy. Soc. Edinb.*, xxviii. 35-57, figs. 11.

DRINKWATER, H. 1912. Account of a family showing minor-brachydactyly. *Compt. Rend. 4e, Conf. Internat. de Genetique, Paris* (1911), 549-562, figs. 14.

DRINKWATER, H. 1914. Minor-brachydactyly, No. 2. *Journ. Genetics*, iii. 217-220, pls. 3.

DRINKWATER, H. 1915. A second brachydactylous family. *Journ. Genetics*, iv. 323-340, pls. 5, figs. 3.

DRINKWATER, H. 1916. Hereditary abnormal segmentation of the index and middle fingers. *Journ. Anat. and Physiol.*, 177-186, figs. 14.

DRINKWATER, H. 1917. Phalangeal anarthrosis (Synostosis, Ankylosis) transmitted through fourteen generations. *Proc. Roy. Soc. Med.*, x. (section Pathology), 60-68, figs. 4.

DUNCAN, F. N. 1917. Orthodactyly. *Journ. Hered.*, viii. 174-175, figs. 2.

ELLSWORTH, H. A. 1917. Inheritance of carpal displacement. *Journ. Hered.*, xviii. 132-133, figs. 2.

FACKENHEIM, J. 1888. Über einen Fall von hereditärer Polydaktylie mit gleichzeitiger erblicher zahnanomalie. *Jena Zeits. f. Naturw.*, xxii. 343-385, figs. 7.

FANTHAM, H. B. 1924. Heredity in man: its importance both biologically and educationally. *S. African Journ. Sci.*, xxi. 498-527, figs. 15.

FANTHAM, H. B. 1925. Some factors in eugenics, together with notes on some S. African cases. *S. African Journ. Sci.*, xxii. 400-424, figs. 4.

FARABEE, W. C. 1905. Inheritance of digital malformations in man. Papers, Peabody Museum, Harvard Univ., iii. 65-78.

FETSCHER, R. 1922. Über die Erblichkeit des angeborenen Klumpfusses. *Arch. f. Rass. u. Gesells.-Biol.*, xiv. 39-52, 140-158.

FORTUYN, A. B. DROOGLEEVER. 1927. A catalogue of the first 400 specimens of the human embryological collection in the Department of Anatomy of the Peking Union Medical College. *Anat. Suppl. China Medical Journ.*, Feb., 1927, pp. 94, pls. 11, figs. 2.

GILMORE, E. R. W. 1927. Hereditary deformity of the fingers. *Brit. Med. Journ.*, ii. 935-936.

HAWKES, ONERA A. MERRITT. 1914. On the relative lengths of the first and second toes of the human foot, from the point of view of occurrence, anatomy and heredity. *Journ. Genetics*, iii. 249-274, pls. 3, figs. 6.

HEFNER, R. A. 1924. Inherited abnormalities of the fingers. I. Symphalangism. *Journ. Hered.*, xv. 323-329, figs. 6.

HEFNER, R. A. 1924. II. Short thumbs (brachymegalodactylism). *Journ. Hered.*, xv. 433-439, figs. 9.

HEFNER, R. A. 1924. III. Subterminal articulation in the proximal joint of the little finger. *Journ. Hered.*, xv. 481-483, figs. 3.

HERZOG, A. 1927. Missbildung im Ellbogengelenk. Eine unbekannte Anomalie. *Fortschr. a. d. Geb. d. Röntgenstr.*, xxxvi. 407-409, figs. 2.

HOFFMAN, H. 1924. Über hereditäre Kolbendaumen. *Klin. Wschr.*, iii. 324, fig. 1.

HOOFF, GERHARD. 1928. Ueber die Erblichkeit der angeborenen Hüftverrenkung. *Arch. f. Rass. u. Gesells. Biol.*, xx. 369-389.

HOWE, FREELAND, JR. 1902. A case of abnormality in cat's paws. *Amer. Nat.*, xxxvi. 511-526, figs. 18.

HURLIN, RALPH G. 1921. A case of inherited syndactyly in man. *Journ. Hered.*, xi. 334-335, figs. 2.

HURST, C. C. 1912. Mendelian heredity in man. *Eugenics Rev* , pp. 25 figs. 6.

INMAN, O. L. 1924. Four generations of symphalangism. *Journ. Hered.*, xv. 329-334, figs. 5.

JACOBSON, A. W. 1928. Hereditary dystrophy of the hair and nails. *Journ. Amer. Med. Assoc.*, xc. 686-689, figs. 11.

JORDAN, H. E. 1911. The inheritance of left-handedness. *Amer. Breeders' Mag.*, ii. 19-29, 113-124.

KEY, J. A. 1927. Hypermobility of joints as a sex-linked hereditary characteristic. *Journ. Amer. Med. Assoc.*, lxxxviii. 1710-1713, figs. 5.

KÖHLER, O. 1924. Ueber die Vererbung der Vielfingerigkeit beim Menschen. *Biol. Zbl.*, xliii. 646-672, figs. 14.

LEWIS, T. 1909*a*. Hereditary malformations of the hands and feet. *Treas. Human Inheritance*, pt. i., 6-10, pls. 3.

LEWIS, T. 1909*b*. Polydactylism. *Treas. Human Inheritance*, pt. i., 10-14, pls. 2.

LEWIS, T. 1909*c*. Brachydactylism. *Treas. Human Inheritance*, pt. i., 14-17, pls. 3.

LEWIS, T., and EMBLETON, D. 1908. Split-hand and split-foot deformities, their types, origin and transmission. *Biometrika*, vi. 26-58, pls. 7.

DE LIMA, J. A. PIRES. 1924. Hereditary atrophy of the nails. *Ann. de Dermat. et Syph.*, v. 266-271, figs. 4.

MACKINDER, D. 1857. Deficiency of fingers transmitted through six generations. *Brit. Med. Journ.*, 845-846.

MCMULLEN, G., and PEARSON, K. 1913. On the inheritance of the deformity known as split-foot or lobster claw. *Biometrika*, ix. 381-390, pls. 6.

MANSON, J. S. 1915. Hereditary syndactylism and polydactylism. *Journ. Genetics*, v. 51-63, pls. 6.

MANSON, J. S. 1928. Observations on human heredity. London: Lewis, pp. 84, pls. 8, figs. 19.

MOHR, OTTO L. 1921. A case of hereditary brachyphalangy utilised as evidence in forensic medicine. *Hereditas*, ii. 290-298, figs. 10.

MOHR, OTTO, and WRIEDT, CHR. 1919. A new type of hereditary brachyphalangy in man. *Carnegie Inst. Wash. Publ.*, No. 295, pp. 64, pls. 7.

MÜLLER, W. M. 1926. Zur Aetiologie des angeborenen Klumpfüsses unter besonderer Berücksichtigung seiner Vererbung. *Arch. d. Julius Klaus-Stiftung*, ii. 1-37.

MURRAY, F. A. 1921. Congenital anomalies of the nails. *Brit. Journ. Dermat. and Syph.*, xxxiii. 409-410, figs. 4.

OLIVER, W. J. 1925. Congenital atrophy of the hair and nails. *Arch. of Derm. and Syph.*, x. 347.

PEACOCK, WESLEY. 1929. Hereditary absence of hands and feet. *Eugen. News*, xiv. 46-47, fig. 1.

PEARSON, K. 1908. On inheritance of the deformity known as split-foot or lobster claw. *Biometrika*, vi. 69-79, pls. 9.

POL, DR. 1921. "Brachydactylie," "Klinodaktylie," Hyperphalangie und ihre Grundlagen. *Virchow's Arch. f. path. Anat. u. Physiol.*, ccxxix. 388-530, figs. 21.

RABAUD, E. 1919. Recherches sur l'hérédité et la variation. *Supp. Bull. Biol. de France et Belg.*, pp. 313.

RAMALAY, F. 1913. Inheritance of left-handedness. *Amer. Nat.*, xlvii. 730-738.

RIEDER, H. 1899. Ueber gleichzeitiges Vorkommen von Brachy- und Hyper-phalangie an der Hand. *Deuts. Arch. Klin. Med.*, lxvi. 330-348, figs. 6.

ROBERTS, ELMER. 1921. Polydactylism in cattle. *Journ. Hered.*, xii. 84-86, figs. 5.

ROCH, GOTTHOLD. 1925. Die Vererbung der sogenannten angeborenen Hüftverrenkung. *Arch. f. Rass.-u. Gesells.-Biol.*, xvii. 241-255.

ROCHLIN, D. G. 1928. Über die hereditäre symmetrische Gelenkhypoplasie. *Zeits. f. Konstitutionslehre*, xiii. 654-663, figs. 4.

SCHMIDT, JOHS. 1920. The genetic behaviour of a secondary sexual character. *Compt. Rend. Trav. Lab. Carlsberg*, xiv., No. 8, pp. 12, pls. 5.

SCHOFIELD, R. 1922. Inheritance of webbed toes. *Journ. Hered.*, xii. 400-401.

SCHROEDER. 1918. Entstehung und Vererbung von Missbildungen an der Hand eines Hypodactyliestammbaumes. *Monatsschr. Geburtshilfe Gynäkol.*, xlviii. 210-222, pls. 3, figs. 7. (From *Bot. Abstr.*, x. 86).

SCHULTZ, A. H. 1922. Zygodactyly and its inheritance. *Journ. Hered.*, xiii. 113-117, figs. 7.

SEDGWICK, W. 1863. On the influence of sex in hereditary disease. *Brit. and Foreign Med.-Chirurg. Review*, xxxi. 445-478, xxxii. 159-197.

SIEMENS, H. W. 1923. Einführung in die allgemeine und spezielle Vererbungspathologie des Menschen. Berlin: Springer, pp. 286, figs. 94.

STAFF, R. 1926. Über eine Familie mit erblicher Syn- und Polydactylie (Hyperphalangia pollicis). *Fortschr. a. d. Geb. d. Röntgenstr.*, xxxiv. 531-538, figs. 90.

STIEVE, H. 1916. Über Hyperphalangie des Daumens. *Anat. Anz.*, lviii. 565-581, fig. 1.

STOCKARD, C. R. 1927. Extra toes in the guinea-pig—an atavistic condition and its genetic significance. *Anat. Record*, xxxv. 24.

STRAUS, W. L., JR. 1926. The nature and inheritance of webbed toes in man. *Journ. Morph. and Physiol.*, xli. 427-439, figs. 19.

SVERDRUP, A. 1922. Postaxial polydactylism in six generations of a Norwegian family. *Journ. Genetics*, xii. 217-240, pls. 6.

TERRY, R. J., and CADY, LEE D. 1923. Comparison of the incidence of the supracondyloid process in groups with normal and abnormal mentality. *Eugenics, Genetics and the Family*, i. 174-177. Baltimore: Williams and Wilkins.

THOMPSON, H. B. 1928. Hereditary dystrophy of the nails. *Journ. Amer. Med. Assoc.*, xci. 1547, figs. 2.

THOMSEN, OLUF. 1927. Einige Eigentümlichkeiten der erblichen Poly- and Syndaktylie bei Menschen. *Acta Medica Scand.*, lxv. 609-644 figs. 8 + 45.

THOMSEN, OLUF. 1927. Nachtrag zu meinem Artikel: Einige Eigentümlichkeiten der erblichen Poly- und Syndaktylie bei Menschen. *Acta Med. Scand.*, lxvi. 588-590, figs. 2.

THOMSEN, OLUF. 1928. Hereditary growth anomaly of the thumb. *Hereditas*, x. 261-273, figs. 12.

TOMESKU, I. 1928. Kongenitale Deviationen der Phalangen. Angeborene Contracturen der Finger und Klinodaktylien. *Arch. f. Orthop. u. Unfall-Chir.*, xxvi. 126-137, figs. 7.

WALTER, A. L., and BRADFORD, W. L. 1928. Congenital familial atrophy of the nails. *Missouri State Med. Assoc. Journ.*, xxv. 20-22.

WEGELIN, CARL. 1917. Über eine erbliche Missbildung des kleinen Fingers. *Berlin. Klin. Wochenschr.*, liv. No. 12.

WILSON, A. G. 1905. Three cases of hereditary hyperkeratosis of the nail-bed. *Brit. Journ. Dermat.*, xvii. 13-14, figs. 3.

WINDLE, B. C. A. 1891. Teratological evidence as to the heredity of acquired conditions. *Journ. Linn. Soc.*, Zool., xxiii. 448-502.

WÖLFFLIN, E. 1926. Über einen Stammbaum von Syndaktylie. *Arch. f. Rass. u. Gesells.-Biol.*, xvii. 412-413.

CHAPTER IX

THE BLOOD GROUPS

SHATTOCK, in 1899, discovered that horse serum to which a drop of human blood has been added produces agglutination of the red corpuscles. Continuing his experiments at St. Thomas's Hospital, he found that the serum from a patient suffering from acute pneumonia and certain other diseases caused clumping of the corpuscles of "normal human blood." He supposed this effect was due to the disease of the patient, and this was the beginning of work on what are now known as the blood groups.

In 1900 Landsteiner discovered that the blood of certain human beings has the capacity of causing hæmolysis in other normal human bloods. Such bloods are said to contain isohæmolysins. These have become of the greatest importance in connection with blood transfusion, since they cause agglutination or clumping of the red corpuscles when the bloods from certain individuals are mixed. The process is now regarded as probably a physical one, by which agglutinins in the blood plasma cause the clumping of the red corpuscles when the latter contain the necessary agglutinogen. These blood differences have since been shown to be inherited, and more recently the proportions in which the agglutinating substances are present in a population are found to be a racial characteristic. An immense literature has thus rapidly developed regarding the blood groups from a medical, genetical and anthropological point of view. This is summarised in Hirszfeld (1928).

Dr. Richard Lower is credited with having performed the first successful blood transfusion in 1665 (see Hollingsworth, 1928), letting out a dog's own blood and letting into its veins the blood from an artery of another dog. The first animal showed no ill-effects. There is a record that Jean Baptiste Denys performed the experiment in France in 1667 of injecting eight ounces of calf's blood into a madman, who survived. Pepys in his *Diary* refers to the experiments—the replacement of a dog's own blood by that of another dog—at Gresham College in 1666; and in the following year of a "frantic" man who had "some of the blood of a sheep let into his body" without

any ill-effects. Lower quickly acquired fame by these experiments, which were taken up in other countries, especially France. At the instance of Robert Boyle, an account of his methods and results was published in *Phil. Trans.*, vol. i.-iii., pp. 353-358.

According to Furuhata (1927, 1928), blood-testing methods, which must have depended upon agglutination reactions, were in vogue in China and Japan as early as the thirteenth century. They are set forth in a Chinese medico-legal book, entitled *Sen-en-roku* (*False Charges cleared*), in 4 vols., by Ji of Sung Dynasty, 1247; also in another work of uncertain date by Cho of the same Dynasty, and in a third work, in 2 vols., called *Mu-en-roku*, or *No False Charges*, by O-Yo of the Gen Dynasty, 1308. The last was translated into Japanese in 1736. In this book the method by which the relationships between two living individuals was tested, was called the blood mixing or blood dropping method. There was also a method called the dropping of blood upon bones, by which the relationship between the living and the dead was determined. Even the Ainu made some sort of blood tests in determining relationship.

After the early transfusion experiments of the seventeenth century, it was quickly found that they were not always successful, and in 1668 they were forbidden in France. In 1818 Blundell revived interest in the subject by experiments on dogs, but progress was slow. The first systematic investigation of the effects of mixing bloods was made by Landois in 1875. Finally, in 1900, Shattock and Landsteiner independently discovered that the serum from certain individuals would agglutinate or clump the red corpuscles of certain others. The frequent previous fatalities were thus accounted for as due to incompatibility of the bloods.

It was soon found that there were two independent substances (rather inappropriately called agglutinogens), named by Landsteiner A and B, either of which might produce agglutination. Landsteiner at first (1901), from isohæmolytic reactions, divided human bloods into three groups. Certain cases were afterwards found which did not fall into these groups, and Jansky (1907) made his classification into four—O, A, B, AB—depending on the presence or absence of two agglutinogens. These specific bodies in the red corpuscles are acted upon by agglutinins in the serum. The blood serum is assumed to contain the corresponding agglutinins, called α and β by von Dungern and Hirszfeld.

Theoretically an agglutinin and the corresponding agglutinogen should not be present in the same individual because their corpuscles would agglutinate. Thus A and α should not coexist, nor B and β, but there are certain facts which indicate that this assumption may be inaccurate. The serum of A agglutinates the red cells of B and the serum of B clumps the red corpuscles of A. In transfusion, fatal effects occur usually only when the corpuscles of the donor are clumped by the plasma of the recipient. It is now being recognised, however (see, *e.g.*, Owen, 1928), that the plasma of the donor may have a serious effect in clumping the corpuscles of the recipient, though this effect will naturally depend upon the amount of blood transfused. In the making of blood tests there are various sources of error, so that the effects in transfusion do not always agree with the tests *in vitro*, in which serum is used for the test. For example, the condition of digestion of the donor may produce partial incompatibility when his blood is otherwise suitable. Also a supposed universal donor may have agglutinins of low titre or strength. For these and other reasons, anomalies occur in some of the collected genetical data.

Individuals of Group O are " universal donors," since their corpuscles are not clumped by any serum. On the other hand, AB individuals are universal recipients; they can take blood from anyone, since their serum will not agglutinate the corpuscles in any type of blood. In tracing the inheritance it has until recently been considered necessary to follow only the agglutinogens A and B. These various relationships are set forth in Table V.

It appears that the inherited entity might equally be designated as the " agglutinogen " A of the red blood corpuscles or the agglutinin α in the plasma. But in inheritance formulæ attention has been fixed on the agglutinogens. The agglutinogens can be demonstrated in blood a long time after death, and they are found in the fœtus as early as the sixteenth week (Koller, 1927). Agglutinins cannot generally be demonstrated so early. They are found in the plasma at birth according to Smith (1928), but these are derived from the mother's blood through the placenta. The maternal agglutinins disappear within a few weeks after birth and the child's own agglutinins only appear in some cases a year or two later.

Koller (1927) tested the blood of 500 women and babes to determine the relationships in the three cases—(1) where the mother's blood agglutinates that of the child; (2) where the

child's blood agglutinates that of the mother; (3) where each agglutinates the other. There was no relation between these conditions and the intoxications of pregnancy. Incidentally certain monozygotic twins were found to belong to the same blood group.

TABLE V

Group.	*Capacity of Red Corpuscles.*	*Effect of Serum.*
I. (O) ..	Not agglutinated by any serum. (No agglutinogen) Universal donor.	Agglutinates cells of Groups II., III., IV. Contains agglutinins α and β.
II. (A) ..	Agglutinated by serum of I. and III. (Contains agglutinogen A).	Agglutinates cells of III. and IV. Contains agglutinin β.
III. (B) ..	Agglutinated by serum of I. and II. (Contains agglutinogen B).	Agglutinates cells of II. and IV. Contains agglutinin α.
IV. (AB) ..	Agglutinated by serum of I., II. and III. (Contains agglutinogens A and B).	No agglutination. Contains no agglutinins. Universal recipient.

In a later paper (1928) Koller and Meier found that the serum of the mother agglutinates the child's blood in every case where this was to be expected from the blood groups of mother and child. The serum of the child, however, agglutinates the mother's blood in only one-third of the cases where agglutination would be expected. It was found that in 12·5 per cent. of heterospecific pregnancies an agglutinin passed from the mother's blood to that of the child.

In 200 cases the blood of the child was tested with the serum of the mother. Always when agglutination was to be expected from their blood groups it happened quickly and clearly. In 100 cases the blood of the mother was tested with serum of the child. In 77 of these cases the reaction of the child's serum was typical. In 16 out of 24 cases the child's blood group lacked the agglutinins to agglutinate the mother's blood. In 4 out of 20 cases the mother's agglutinins were weakly present in the child's serum, so that *in vitro* agglutination of the child's own blood by its serum took place. In only 7 out of 24 cases were

agglutinins against the mother's blood present in the child's serum.

Thus human bloods have been classed into four groups according to whether either or both or neither of these agglutinogens was present. Jansky (1906-07) classified them as follows: Group I.=O, Group II.=A, Group III.=B, Group IV.=AB. This nomenclature should be universally followed, and will be adopted here. Moss (1910) independently proposed a grouping which differed in that Group I. was AB and Group IV. O. This is still followed in much medical and hospital work, but should be discarded in order to avoid confusion. The danger and confusion arising from the existence of two such systems of symbols is very serious.

Von Dungern and Hirszfeld (1910) tested 348 persons belonging to 72 families, and showed that the blood groups were inherited as Mendelian differences. They concluded that the isohæmagglutinogens A and B are each dominant to their absence, the Group O being double recessive and AB double dominant; hence two independent pairs of factors would be involved. This view was held for a decade, and a number of papers (*e.g.*, Learmonth, 1920; Ottenburg, 1923) on inheritance of the blood groups were founded upon it. Some results, however, did not fit in with this scheme, and it was denied by Koltzoff (1921). Bernstein (1925), from a statistical study of the data of inheritance, proposed a multiple allelomorph hypothesis, which was confirmed by Furuhata (see Furuhata, 1927), according to which A and B are allelomorphic to each other. This is supported by Snyder (1926*a*) on the basis of a study of 200 families in North Carolina.

Bernstein, using the published results, found that in a total of 310 families with 1,350 individuals the multiple allelomorph hypothesis was only contradicted by the recorded condition of 11 persons in 6 families. An endeavour is made to explain away these few exceptions.

Bernstein (1925) showed mathematically that the proportions of the four types in a population are not in accord with expectation on a two factor hypothesis. Only the agglutinogens are considered in his formulæ. Thus, naming the genes A, B, R (absence of both), we have six blood classes—

	RR	RA AA	RB BB	AB
Class	O	A	B	AB

Using p, q, r, as the frequency respectively of the genes A, B, R, in a population; then $p+q+r=1$, and the probability for the frequency of the six genotypes will be—

RR	BR	BB	AR	AA	AB
r^2	$2qr$	q^2	$2pr$	p^2	$2pq$

The probabilities for the four groups are then—

Group	$\bar{O}=RR.$	$\bar{B}+BR=BB.$	$\bar{A}=AR+AA.$	$\overline{AB}=AB$
Probability	r^2	$2qr+q^2$	$2pr+p^2$	$2pq$

From which it may be shown that in a population

$$1=p+q+r=1-\sqrt{\bar{O}+\bar{B}}+1-\sqrt{\bar{O}+\bar{A}}+\sqrt{\bar{O}}.$$

Using this formula, the proportions of the four groups are in better accord with those actually found in various populations.

Snyder (1925) assumes that the recessive agglutinins are primitive and that the dominant agglutinogens arose from them by mutation. It has usually been assumed that originally human blood uniformly lacked agglutinogens, these substances arising in the corpuscles later as the result of mutations. Different views are held regarding the single or multiple origin of the various blood elements. If the plasma arises from the corpuscles, then the agglutinins would be secondary, but some hold that they come from different sources. In chick embryos the power of shed blood plasma to agglutinate red corpuscles is absent before the eleventh day of incubation, but on the twelfth day the plasma has some power of agglutinating the erythrocytes of other species (Pickering, 1928).

The view of multiple allelomorphs, which has been rather widely accepted, still presents certain difficulties. Both views assume that the human race was originally O, and that A and B arose as the result of different mutations in the germplasm. The results of the various crosses according to the two theories may be seen in the following table taken from Hirszfeld (1928).

Thus it is in crosses involving an AB individual that the blood groups of the offspring would differ, since according to the two-factor hypothesis A and B would be situated in different chromosomes, while the multiple allelomorph hypothesis would place them at the same locus in the two members of a single pair of chromosomes. There are various sources of error, founded partly on the technique of taking the blood groups and partly on mistaken parentage, and very few of the inheritance data so far collected are quite free from exceptions

to either rule. According to Ottenberg's two-independent-factor hypothesis the AB group would include four genotypes, AABB, AaBB, AABb, and AaBb, while in the three-allelomorph hypothesis there would be only one genotype AB.

TABLE VI

Parents.	*Expected Offspring.*	
	Two Pairs of Factors.	*Three Multiple Allelomorphs.*
O × O	O	O
O × A	O, A	O, A
O × B	O, B	O, B
A × A	O, A	O, A
B × B	O, B	O, B
A × B	O, A, B, AB	O, A, B, AB
O × AB	O, A, B, AB	A, B
A × AB	O, A, B, AB	A, B, AB
B × AB	O, A, B, AB	A, B, AB
AB × AB	O, A, B, AB	A, B, AB

According to the two-factor hypothesis, the following genotypes may occur according to whether the individual is heterozygous or homozygous for one or both factors.

TABLE VII

Group.	*Phenotype.*	*Genotype.*
I.	O	aabb
II.	A	AAbb, Aabb
III.	B	BBaa, Bbaa
IV.	AB	AABB, AaBB, AABb, AaBb

On the multiple allelomorph hypothesis the AB group could have only one genotype instead of four. To follow a strictly genetic nomenclature, one should write AA^1 as the multiple allelomorphs, instead of AB, but since the letters A and B have been widely applied to the two agglutinogens, both in anthropological and medical literature, it seems best not to change this usage now, especially since A and B appear to have had different histories in the human race (*vide infra*). According to the scheme proposed by Bernstein (1925), the formulæ for the agglutinogens of the various blood types would be as follows (Table VIII.) :

TABLE VIII

Group.	*Phenotype.*	*Genotype.*	
I.	O	RR	—
II.	A	AA	AR
III.	B	BB	BR
IV.	AB	AB	—

Bernstein has shown mathematically that the presence of two independent pairs of Mendelian factors in a population would give different proportions of the four groups from those actually found in populations.

Furuhata (1927), after determining the blood groups in 958 Japanese families involving 3,951 persons, adopts the conception that the corpuscle and serum characters are inherited in couples. Those of the red corpuscles he represents by A and B, those of the serum by a and b. In following this notation it must be recognised that a does not represent the absence of A, but a complementary condition present with A in the blood of the individual. According to this view there are three inheritable allelomorphs ab, Ab and aB, each of which can be inherited through egg or sperm. Thus there will be three types of homozygous individuals ab.ab, Ab.Ab and aB.aB, and three heterozygotes, Ab.ab, aB.ab and Ab.aB. This gives the scheme of six blood groups in Table IX.

TABLE IX

FURUHATA'S GENE-SCHEME.

Jansky's Classification.	*Phenotype.*	*Genotype.*	
		Homozygote.	*Heterozygote.*
Group I.	O	ab.ab	—
„ II.	A	Ab.Ab	Ab.ab
„ III.	B	aB.aB	aB.ab
„ IV.	AB	—	Ab.aB

Bernstein (1925) and Hirszfeld (1928) both hold that the isoagglutinins should not be considered in connection with the inheritance of the agglutinogens, and that the sera of the three blood types are not necessarily differentiated. In any case the inheritance of the agglutinins requires further investigation. Hirszfeld adheres to the theory of two independent factors.

He cites studies of over 5,000 children and their parents, in which only 36 (0·6 per cent.) are not in conformity with expectation. These are explained by faulty technique or illegitimacy.

A very recent development has taken place in the theory of blood group inheritance, which appears to resolve the difficulties in the two previous theories. H. K. Bauer (1928) proposes the hypothesis of two factors with crossing-over, and finds it in harmony with the available statistics of blood groups in parents and children (Table X.).

TABLE X

Parents.	*No. of Fams.*	*Blood Groups of Children.* O		A		B		AB		*No. of Children.*
		Abs.	*Per Cent.*	*Abs.*	*Per Cent.*	*Abs.*	*Per Cent.*	*Abs.*	*Per Cent.*	
O×O	491	1,164	99·3	8	0·7	—	—	—	—	1,172
A×A	493	221	18·1	1,002	81·9	—	—	—	—	1,223
B×B	134	56	17·2	—	—	269	82·9	—	—	325
O×A	1,018	985	41·7	1,357	57·6	11	0·4	8	0·3	2,361
O×B	450	438	41·7	3	0·3	607	57·9	1	0·1	1,049
A×B	513	198	17·3	346	30·2	318	27·8	282	24·7	1,144
O×AB	174	26	5·5	216	45·6	204	43·0	28	5·9	474
A×AB	173	10	2·3	200	45·6	103	23·6	125	28·5	438
B×AB	93	7	2·8	53	21·0	122	48·5	70	27·8	252
AB×AB	29	—	—	15	23·4	17	26·6	32	50·0	64
	3,568	3,105	36·5	3,200	37·7	1,651	19·4	546	6·4	8,502

Thus in O×AB he finds a cross-over value of 11·4 per cent. The results, and their comparison with expectation, are shown in Table XI.

TABLE XI

O×AB	*Blood Groups of Children in per Cent.* O	A	B	AB
Without crossing-over ..	—	44·5	44·5	—
With 11 per cent. " ..	5·5	44·5	44·5	5·5
Actual results	5·5	44·6	43·0	5·9

Similarly for the other crosses, A × AB, etc., the results appear to compare favourably with expectation.

Owen (1928) emphasises that agglutination is not always according to expectation on the four group hypothesis, and that the effect of the donor's plasma must always be considered. He believes there is evidence of three pairs of agglutinable elements, and others have obtained indications of something similar.

The blood groups have recently been used as an additional test of identical twins. Wiechmann and Paal (1928) find that in twelve pairs of twins identical according to Siemens' tests, the twins belonged to the same blood group, while of twelve pairs of duplicate twins three belong to different blood groups. Keynes (1927) cites a pair of supposedly identical twins, one of which belonged to Group II. and the other to Group IV. (of Moss). But the fact that they were used to replace each other in a " stage mystery " is not sufficient evidence that they were really uniovular.

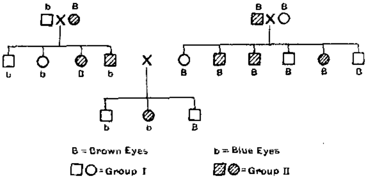


FIG. 56.—BLOOD GROUPS AND EYE COLOUR. (After Snyder.)

Many papers have been written to show that linkage occurs between particular blood groups and certain pathological conditions; but Snyder (1926) has shown that genetic linkage is a much more difficult thing to prove than these authors had supposed. Considering the large number of chromosomes in man (see p. 21), free assortment of any pairs of characters studied is much more likely to occur than linkage between them. The difficulties of studying linkage are increased by the small number of offspring in families and by the absence of controlled matings, but certain conclusions may be drawn from the study of three generations in a number of pedigrees.

As an example of the method, Snyder gives a pedigree (Fig. 56) in which the blood groups and eye colour are recorded for three generations of a family.

Free assortment is indicated by the readiness with which the factor pairs separate, but much further evidence would be required before any conclusions regarding the presence or absence of linkage could be drawn.

Attempts have been made to show that hæmophilia, malignant disease, carcinoma, atopic hypersensitiveness, susceptibility to diphtheria and goitre, and other abnormalities are linked to particular blood groups, but there is at present no proof of such linkage in any case. Snyder (1926) found normal distribution of the blood groups among cases of feeble-mindedness, epilepsy and dementia præcox—*i.e.*, the proportion of the blood groups did not differ among these people from those in the normal population. He has since (1928) shown that the blood groups are independent of eye colour, direction of occipital whorl, susceptibility to Schick test, susceptibility to goitre and migraine. Snyder points out that in the case of any character, free assortment with the blood groups might (and usually will) occur, or partial or complete linkage, or one blood group might by its presence conceivably affect some pathological or anatomical condition in the body. Up to the present, however, the blood groups represent purely biochemical conditions of the blood which have no relation to any other known character or condition. They are independent of age, sex, vocation, disease, drugs, anæsthesia, Röntgen rays, climate or living conditions.

The Serological Races of Man.

The inheritance of the blood groups is a purely genetical problem, but the subject soon took on wider racial and anthropological aspects when it was found that different races and populations were characterised by different frequencies of the four groups. Large numbers of records have been taken, to determine the ratios of the four groups for different countries. This work was begun by the Hirszfelds (1919) on soldiers of different nationalities during the war. Working on troops in the Macedonian army in Serbia, they found that all human races present some A and some B, but that there is a great preponderance of A in European and of B in Asiatic and African races. From these facts they drew the inference that the human race originally possessed neither A nor B, that B arose on the central Asian plateau as a mutation in prehistoric times, while A appeared in Northern Europe. The present

mixtures would then be due to subsequent migrations and intermingling of races. A few typical cases of the group frequencies in different races are given in Table XII. from the large number of records brought together by Hirszfeld (1928).

TABLE XII

Population.	*Number Tested.*	*Groups, in per Cent.*			
		O	*A*	*B*	*AB*
English (Liverpool)	1,600	46·0	30·0	17·0	7·0
Americans	5,000	44·4	36·0	14·2	5·1
Germans (Schleswig-Holstein) ..	3,156	40·7	41·3	12·5	5·3
Finns	5,134	32·8	43·5	17·0	6·7
Russians (Moscow)	2,200	32·0	38·5	23·0	6·5
Poles	11,488	32·5	37·6	20·9	9·0
Lapps (Sweden)	404	28·9	62·6	4·5	4·0
Japanese	1,786	30·2	37·9	22·5	9·5
Chinese	1,000	30·0	25·0	35·0	10·0
Buryats	1,542	30·4	21·9	37·8	9·9
Manchurians (Mukden)	236	30·9	25·9	33·9	9·3
Hindoos (India)	228	31·8	18·5	40·9	8·7
Gypsies (Hungary)	385	34·2	21·1	38·9	5·8
Australian natives	1,176	52·6	36·9	8·5	2·0
Melanesians (New Guinea) ..	753	53·7	26·8	16·3	3·2
Negroes (W. Africa)	325	52·3	21·5	23·0	3·2
Indians (N. America)	1,104	79·1	16·4	3·4	0·9

The statistics vary considerably when taken from different parts of the same country, but in general it will be seen that the percentage of A is high in Western Europe, while B is high in Southern and Eastern Asia, there being a gradual fall of A and rise of B in passing eastward. B is most frequent in Buryats, some Chinese and Hindoos. The Gypsies of Hungary still have the same proportion of blood groups as natives of India, although they are believed to have migrated from India in the twelfth century.

Various attempts have been made by Ottenberg, Snyder and others to group human races into "types," such as Indo-Manchurian, Hunan, and European, but all such types are purely arbitrary and of little value. It seems clear that intermingling of races has been going on throughout human history and prehistory. Since European populations in general are

high in A, while the populations of Eastern and Southern Asia are high in B, it has been assumed that these were the respective regions of origin of the agglutinogens, which have since been dispersed by migrations and crossing of races.

The percentage of Group I. (O) may also be regarded as a measure of racial isolation. In some statistics of North American Indians, the percentage of O for Indians believed to be of pure blood runs as high as 91·3 per cent., and it may be that before the advent of the white man they were all O. This is in accord with the early passage of the Indians over the Behring Straits. Australian natives, Melanesians, and African negroes are also high, though less so, in O, and the two former have a high percentage of A. A is therefore in general more widespread, and hence older, than B. The earlier origin of A is also supported by the absence of B from the Amerinds, although North-Eastern Asia, in their path of migration, is now occupied by races high in B. These arguments have recently been set forth elsewhere (Gates, 1929) as showing that B was later to appear than A. Bernstein (1928) has independently reached the same conclusion on somewhat different grounds.

Blood grouping has thus become an important criterion of racial relationships in man. Many races remain to be tested, and the work is actively going on all over the world. There are certain cases in which the blood grouping may form a very strong argument for independent racial origin, but it is not necessary to follow these anthropological questions further here. The importance of the blood groups lies in the fact that, although invisible, they behave as units in crossing. Hence while the physical results of crossing may be obscured or lost by "blending" owing to the recombination of innumerable differences, the blood groups persist as evidence of an earlier cross. This opens an immense field for the determination of blood groups in hybrid races. It may be pointed out that S. Shirai (1922, 1923, 1924, Japanese, cited by Furuhata) has reported that human sperm and saliva are also in four groups like the blood.

Young (1928) has recently brought out certain further relationships. He applies Pearson's χ^2 test to a large series of published results of racial blood tests and finds that by this means percentages which look very similar are nevertheless often significantly different. Thus he differentiates not only the Poles from the Japanese and the Russians from the Chinese, but he also finds the Germans of Schleswig-Holstein

significantly different from those of Leipzig, the Roumanians of the mountains different from those of the valleys, as well as differences in the Ainu from differing localities. On the other hand, he finds that the European types, Nordic, Mediterranean, and Alpine, do not show any differentiation of their blood-group frequencies, although some anthropologists consider them as distinct as Australian, negro, and Mongol. If, however, as is historically known to be the case, different races and tribes have been intermingling in the European area for thousands of years, a general uniformity in blood groups over the area taken as a whole, combined with local differences, might perhaps be expected. The fact which Young points out, that the blood grouping of Australian whites and the native blackfellows is not significantly different, appears to be satisfactorily explained if one assumes that A is considerably earlier in origin than B (see Bernstein, 1928; Gates, 1929). It may be further stated that according to some results (Cleland, 1926) B is absent from pure-blooded Australian aboriginals, as it is also from the North American Indians, which is in accord with an earlier dispersion of these races, before B appeared. The chance similarity in blood grouping of Egyptians and Ainu, of Russians and American negroes has no significance if one adheres to the hypothesis that A and B when they appeared were widely separated both in time and space.

In a series of papers by Landsteiner and Miller in 1925 they have shown that the blood of the anthropoid apes contains specific group elements identical with those of man. Of 14 chimpanzees investigated, three belonged to Group O and 11 to Group A.* Of orang-utans tested, two were A, three B and one AB. One gibbon examined belonged to Group A. Lower monkeys were also tested—76 individuals belonging to 36 different species: 46 of these, which belonged to 18 species of Cercopithecidæ (Old World monkeys), showed neither A nor B; but 22 belonging to the Platyrrhinæ (7 genera) gave the B reaction, as did also 8 individuals belonging to six different families of Lemuroidæ. The isoagglutinin B in these monkeys and lemurs is like that of human blood, but not identical with it. Hence, so far as examined, it appears that the lemurs and platyrrhine monkeys contain only B, while the chimpanzee has A and the orang both. It is possible, however, that geographical differences may also develop in the anthropoids with

* Von Dungern and Hirszfeld examined three more which they placed in Group A.

further investigations. In any case the presence of A and B in the apes does not necessarily mean that man derived his agglutinogens from anthropoid ancestors. It seems equally likely at present that they represent independent parallel mutations in the anthropoid and the human line of descent. If this is not the case, it is difficult to see how the blood groupings of different human races can be significant as showing racial relationships.

Landsteiner (1928) has recently made further observations. A total of 55 chimpanzees has now been tested, 50 of which were A and 5 in Group O. This high percentage of A is very striking. On the other hand, it was not possible to assign the blood of a gorilla to one of the four groups. It was easy to distinguish human blood from that of the anthropoids.

It may be added that Hirszfeld has examined 45 horses serologically, finding 30 per cent. O, 55 per cent. A, and 15 per cent. B.

Finally, Landsteiner and others have shown the presence of "cold" agglutinins in human blood, which produce their agglutinating effects chiefly at low temperatures. Recently Landsteiner and Levine (1928) have shown the presence of two entirely independent agglutinable structures which they call M and N. They have been studied in 166 families and appear to behave (like A and B) as a pair of dominant factors, allelomorphic or closely linked. Among 1,708 white individuals, 19·1 per cent. were negative for M, and among 532 26·1 per cent. were negative for N.

Doubtless much remains to be learned of the blood groups and their inheritance in other animals. Ionesco-Mihaiesti and Dumitesco (1928) have studied the blood groups in rabbits. They find that there are two isoagglutinogens, which they call A and B, A being much more frequent. Among 331 rabbits tested, only two contained B. In the few cases when the isoagglutinin B is present they find that it is always accompanied by A, and so they derive five blood groups in rabbits, as follows:

	Serum.	*Corpuscles.*
I.	ab	O
II.	a	O
III.	o	A
IV.	a	B
V.	o	O

LITERATURE

BAUER, K. H. 1928. Zur Lösung des Problems der Blutgruppenvererbung. *Klin. Wochenschr.*, vii. 1588-1592.

BERNSTEIN, FELIX. 1924. Ergebnisse einer biostatischen zusammenfassenden Betrachtung über die erblichen Blutstrukturen des Menschen. *Klin. Wochenschr.*, iii. 1495-1497.

BERNSTEIN, FELIX. 1925. Zusammenfassende Betrachtungen über die erblichen Blutstrukturen des Menschen. *Zeits. f. ind. Abst. u. Vererb.*, xxxvii. 237-270.

CLELAND, J. B. 1926. Blood-grouping of Australian aboriginals. *Austral. Journ. Exp. Biol. and Med. Sci*, iii. 33-35.

VON DUNGERN AND HIRSZFELD, L. 1910. Über Vererbung gruppensspezifischer Strukturen des Blutes. *Zeits. f. Immun. exp. Therapie*, vi. 284.

FURUHATA, T. 1927. On the heredity of the blood groups. *Japan Medical World*, vii., No. 7, 1-13.

FURUHATA, T. 1928. On the heredity of the blood groups. *Verh. V. Internat. Kongr. Vererb.*, i. 705-735, pls. 3.

GATES, R. R. 1929. Blood groups of Canadian Indians and Eskimos. *Amer. Journ. Phys. Anthrop.*, xii. 475-485.

HIRSZFELD, L. and H. 1919. Serological differences between the blood of different races. *Lancet*, ii. 675-679.

HIRSZFELD, L. 1928. Konstitutionsserologie und blutgruppenforschung. Berlin: Springer, pp. 235, figs. 12.

HOLLINGSWORTH, M. W. 1928. Blood transfusion by Richard Lower in 1665. *Annals of Med. History*, x. 213-225, figs. 3.

IONESCO-MIHAIESTI, C., and DUMITRESCO, D. 1928. Groupes sanguins chez le lapin. *Compt. Rend. Soc. Biol.*, xcviii. 1637-1638.

JANSKY. 1906. Hämatologische Studien bei Psychotikern. *Kliniky sbornik*, 1906, No. 2.

JANSKY 1907. *Jahresber. f. Neurol. u. Psychiatrie*, 1907, 1028

KEYNES, G. 1927. The blood groups of identical twins. *Lancet*, ccxii. 459-460.

KOLLER, THEO. 1927. Untersuchungen über das Verhältnis der Blutgruppen bei Müttern und ihren Neugeborenen, mit spezieller Berücksichtigung der gegenseitigen Isoagglutination. *Arch. d. Julius Klaus-Stiftung*, ii. 247-272.

KOLLER, THEO, and MEIER, U. M. 1928. Isoagglutinine im Serum der Neugeborenen. *Arch. f. Klaus-Stiftung*, iii. 219-238.

KOLTZOFF, N. 1921.

LANDSTEINER, K. 1900. Zur Kenntnis der antifermentativen, lytischen und agglutinierenden Wirkung des Blutserums. *Zentbl. f. Bakt. Parasit. i. Infekt.*, xxvii. 361.

LANDSTEINER, K. 1901. Über Agglutinationerscheinungen normalen menschlichen Blutes. *Wien. Klin. Wochens.*, xiv. pt. 1, 132.

LANDSTEINER, K. 1928. The human blood groups. *The Newer Knowledge of Bacteriology and Immunology*, chap. lxviii, 892-908, figs. 2.

LANDSTEINER, K. 1928. Sur les propriétés sérologiques du sang des Anthropoïdes. *Compt. Rend. Soc. de Biol.*, xcix. 658.

LANDSTEINER, K., and LEVINE, PH. 1926. On the cold agglutinins in human serum. *Journ. Immunol.*, xii. 441-460.
LANDSTEINER, K., and LEVINE, PH. 1928. On the inheritance of agglutinogens of human blood demonstrable by immune agglutinins. *Journ. Exp. Med.*, xlviii. 731-749.
LANDSTEINER, K., and MILLER, C. P., JR. 1925. Serological studies on the blood of the primates. I. The differentiation of human and anthropoid bloods. *Journ. Exp. Med.*, xlii. 841-852.
LANDSTEINER, K., and MILLER, C. P., JR. 1925. II. The blood groups in anthropoid apes. *Journ. Exp. Med.*, xlii. 853-862.
LANDSTEINER, K., and MILLER, C. P., JR. 1925. III. Distribution of serological factors related to human isoagglutinogens in the blood of lower monkeys. *Journ. Exp. Med.*, xlii. 863-872.
LANDSTEINER, K., and WITT, D. H. 1926. Observations on the human blood groups. Irregular reactions. Isoagglutinins in sera of Group IV. The Factor A^1. *Journ. Immunol.*, xi. 221-247.
LEARMONTH, J. R. 1920. The inheritance of specific isoagglutinins in human blood. *Journ. Genetics*, x. 141-148.
OTTENBERG, R. 1923. Hereditary blood qualities: statistical considerations. *Journ. Immunol.*, viii. 11.
OTTENBERG, R. 1925. A classification of human races based on geographic distribution of the blood groups. *Journ. Amer. Med. Assoc.*, lxxxiv. 1393-1395.
OWEN, J. LEWIS. 1928. Some observations on blood grouping. *Edin. Med. Journ.*, xxxv. 222-235.
PICKERING, J. W. 1928. The blood plasma in health and disease. London: Heinemann, pp. 247.
SHATTOCK, S. G. 1899. Chromocyte clumping in acute pneumonia and certain other diseases, and the significance of the buffy coat in the shed blood. *Trans. Pathol. Soc. London*, l. 279-293. *Journ. Path. and Bacteriol.*, vi. 303-314.
SMITH, C. H. 1928. Isoagglutinins in the blood of the newborn, with special reference to their placental transmission. *Amer. Journ. Diseases of Children*, xxxvi. 54-69.
SNYDER, L. H. 1924. The inheritance of the blood groups. *Genetics*, ix. 463-478.
SNYDER, L. H. 1925. Human blood groups and their bearing on racial relationships. *Proc. Nat. Acad. Sci.*, xi. 406-407.
SNYDER, L. H. 1926. Studies in human inheritance. I. The linkage relations of the blood groups. *Zeits. f. Immunitat. u. exp. Therapie*, xlix. 464-480, fig. 1.
SNYDER, L. H. 1926. Human blood groups: their inheritance and racial significance. *Amer. Journ. Phys. Anthrop.*, ix. 233-263, figs. 2.
SNYDER, L. H. 1927. Blood grouping and its practical applications. *Arch. Path. and Lab. Medicine*, iv. 215-257, figs. 5.
SNYDER, L. H. 1928. The linkage relations of the blood groups. *Verh. V. Internat. Kongr. Vererb.*, ii. 1393.
WIECHMANN, E., and PAAL, H. 1927. Die Blutgruppenbestimmung in ihrer Bedeutung für Zwillingsforschung. *Münch. med. Wochenschr.*, lxxiv. 271.
YOUNG, MATTHEW. 1928. The problem of the racial significance of the blood groups. *Man*, xxviii. 153-159, 171-176.

CHAPTER X

DISEASES OF THE BLOOD SYSTEM

AMONG abnormalities of the blood *hæmophilia* takes a leading place, although new diseases relating to the blood are constantly being described. Sir H. Rolleston (1928) has discussed the hereditary factor in various diseases of the hæmopoietic or blood-forming system. He points out that in hereditary pseudo-hæmophilia and hereditary thrombopenia both sexes are affected, in contrast to hæmophilia, which is male-sex-linked. Hæmophilia was first characterised by John C. Otto in Philadelphia in 1803, but as early as 1519 Albucasis described men who bled to death when not severely wounded. From statements in the Talmud regarding circumcision in certain families, it is evident that there were hæmophilics in ancient Jewish families. The many pedigrees, some of them very extensive, all show essentially the same type of inheritance, with variations in minor details—*i.e.*, transmission as a recessive sex-linked character by females in hæmophilic pedigrees to half their sons. This is the so-called "law of Lossen," who described the famous Mampel family from near Heidelberg in 1877, and denied that affected males transmit the disease. The "law of Nasse" (1920) affirmed that the daughters of affected males are also transmitters. The usual absence of male transmission results merely from the fact that hæmophilic males usually die without leaving progeny, and if this had been realised much unnecessary controversy would have been avoided. It is only necessary to remember that the disease is determined by an X-chromosome which carries the defect (see p. 23).

Schloessmann (1924), in an extensive review of hæmophilic families in Württemberg, confirms that all pedigrees show sex-linkage. He also concludes that all women who show symptoms of hæmophilia are transmitters, and that no woman shows the typical condition as it occurs in man. There is only a partial expression of the latent defect, as shown by an increased coagulation-period. An accurate method of measuring coagulation-time is important. It is normally 4 to 8 minutes, but in

hæmophilics may be as much as two hours, and it varies in different families. In certain families the hæmophilic phenomena may only appear some hours or days after a wound. Schloessman finds greater fertility in hæmophilic families, which he attributes to the early death of many children and the desire to leave offspring. Weinberg (1925) finds that in one hæmophilic family in Württemberg female carriers show no delay in the coagulation-time. He concludes that when delay occurs in carriers it is due to other elements of the inherited constitution.

Hæmophilia is common in the Black Forest, in mountain valleys and small isolated villages. Schloessmann studied 24 families (1,596 persons), following some of them through six or seven generations. The largest pedigrees are the Kiefer (298) and Bott (219) families, which are interrelated and make a complex of 517 individuals. The next largest are Hössli's (about 400) and Lossen's (Mampel) family with 213. Five cases of " sporadic " hæmophilia are cited. In one the pedigree includes large families in two generations with a single hæmophilic, giving strong evidence of a *de novo* origin. In another large pedigree in six generations it appears in two brothers of the fifth generation. In this case the germinal origin would have been in the mother. She had ten brothers, all normal, so her mother could scarcely have been a transmitter. In another pedigree three brothers in the third generation are bleeders. Their mother's mother, who should have been a carrier, had five healthy brothers, some of whom should have shown the condition if it was in the germplasm of this family. But the mother of the three brothers had strong nosebleed as a girl, and one of their sisters bled abnormally from the skin and under the skin from slight scratches. Hence the condition was probably not new in the family. In another case the mother of two bleeders bled unusually copiously in menstruation and at childbirth. This is characteristic of some women carriers, and Schloessmann believes that women carriers can be detected by the time of coagulation.

That bleeders can transmit, is now proved by a number of cases. Pedigree XIX. of Schloessmann contains a case of a hæmophilic father transmitting it to his daughter's son. In the Kiefer pedigree, a bleeder born in 1798 married twice, and by each wife transmitted hæmophilia through the daughters to later generations. One at least of the female descendants of this family bled from the nose and teeth, showed blue marks under

the skin and had a slow clotting-time. Female " bleeders " only occur in the Calmbach complex of families, yet the women in other pedigrees frequently show such a tendency, and every carrier tested was found to have an increased coagulation-time. Nevertheless, the complete phenomena of hæmophilia do not show in women, as they would lead to death if present. Formerly, cases in which a male bleeder appeared to transmit hæmophilia were explained away by assuming the wife to be a carrier, or in some other way. But since all his sperm will carry the defective X-chromosome, it is obvious that if he has any female children they must all be transmitters. Complete sterility is the only thing which would prevent such transmission. On the other hand, he cannot transmit to a son, because a son does not get an X-chromosome from his father.

Bulloch and Fildes (1910), in their monograph on hæmophilia, bring together a vast amount of information and many pedigrees. In the 44 families studied there were 644 males and 464 females—a great excess of males. The marriage-rate of males in bleeder families is very much lower than of females (9·6 per cent. : 36·8 per cent.). They concluded that cases described as female hæmophilics were really hæmorrhagic. Lenz (1912) gives an extensive bibliography of hæmophilia.

Bauer and Wehefritz (1924) give a number of pedigrees of hæmophilia and *thrombopenia* (a deficiency of thrombocytes in the blood). The latter is a simple dominant, appearing in either sex in all generations, and needs to be carefully distinguished clinically from true hæmophilia. Some supposed female " bleeders " are cases of thrombopenia.

Warde (1923) traces a pedigree of hæmophilia with 12 cases in five generations (Fig. 57). In the seventh generation the family contained seven normal daughters and seven sons, four of whom were hæmophilic. The propositus (IV. 8), as a girl of ten, was found unconscious through loss of blood from a tooth extraction. Afterwards she had severe hæmorrhage from a cut thumb, and on another occasion bled for two weeks after opening an abscess. She was easily bruised, and when her hæmophilic son was born she suffered from hæmorrhage. The son died from bleeding at the age of five years. The coagulation-time of this woman was 3 to 3·35 minutes at 37° C. After special treatment she survived an operation for carcinoma of the breast, but the wound bled for three weeks. This woman no doubt had hæmophilia in a reduced and sub-lethal form.

Weinberg (1924) suggested in 1912 that homozygous female

bleeders (there can be no such thing as a homozygous male bleeder, because the male has only one X-chromosome) were non-viable. This would account for the absence of female bleeders showing the full symptoms. He prefers the term lessened viability to the terms lethal factor or deficiency. Little and Gibbons (1921) made the same suggestion, and Mohr (1926) has reached the same conclusion from a study of the mortality in a group of cases. Nevertheless it is still denied by some. B. Lloyd (1925) describes an American family and a Russian family, each of four generations, in which bleeding is accompanied by swelling of the joints followed by discolora-

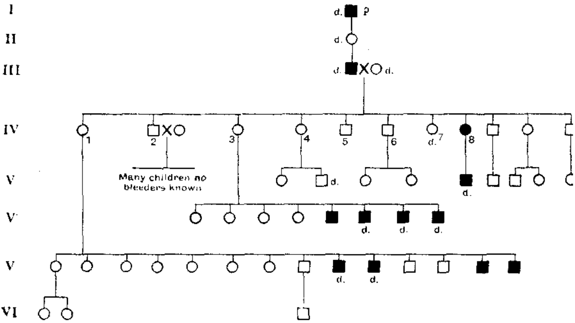


FIG. 57.—PEDIGREE OF HÆMOPHILIA. (After Warde.)

tion and pain, no doubt due to internal bleeding. The condition is incompletely recessive in heterozygous females, who show the symptoms, but less than males. One such woman who was a "pronounced bleeder" had a normal son, showing that she must have been heterozygous for the condition.

Klug (1926) has recently published a further account of the famous Mampel family, the sixth generation of which is now growing up. The Mampels themselves no longer exist in Kirchheim, its descendants having emigrated to America, where nothing further is known of them. But the Teutsch and Wendling families, descended respectively from Elizabeth Mampel (born 1821) and Anna K. Mampel (born 1830), have

been followed in two pedigrees (see Fig. 58). Of the 52 families in this descent, only 12 have hæmophilia, and in these only the males show abnormal bleeding phenomena. Klug points out mistakes of Lossen, whose scheme showed 37 bleeders where there were really only 23 (including four in the younger generation). This was because the others said they were bleeders in order to escape military service. The bleeding propensity is stronger in some branches of the family than in others. These pedigrees include but one true bleeder-father (IV. 8), who had three normal daughters and a normal son. But there is no reason to doubt that these daughters would all

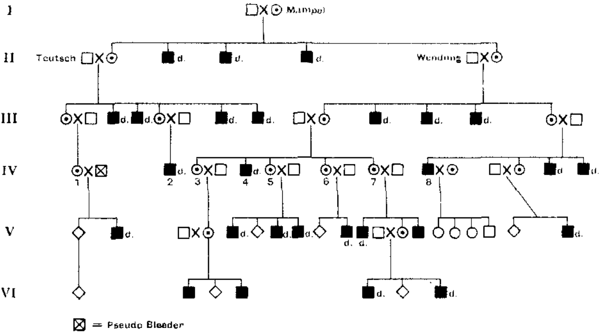


FIG. 58.—PEDIGREE OF HÆMOPHILIA. (After Klug.)

be carriers. The modern families are smaller than formerly, and there is no excessive fertility. K. H. Bauer, from a study of 233 hæmophilic pedigrees, including the Mampel family, concluded that the homozygous female is lethal. Klug disagrees with this, but points out a discrepancy from expectation in that *all* the women in the Wendling family are carriers, and this can hardly be merely chance. But in the whole Mampel family there are 66 sons, of whom 27 are bleeders and 39 normal; and 58 daughters, of whom 14 are carriers and 10 not (as yet), the remainder not having had children.

An interesting pedigree of hæmophilia in an American family is described by Davidson and McQuarrie (1925).

Eight generations descended from the marriage of a Quaker woman named Jasper to Sir William Crispin in 1746 contain

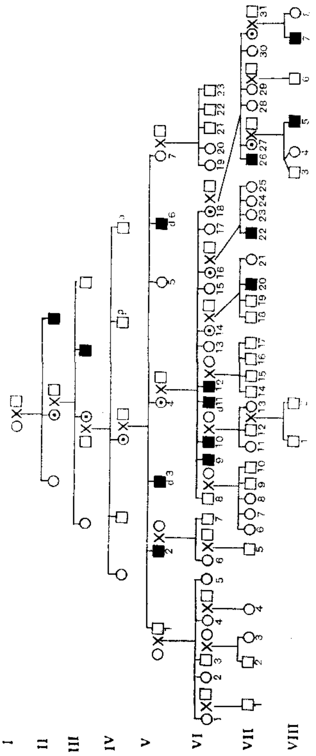


FIG. 59.—PEDIGREE OF HÆMOPHILIA. (After Davidson and McQuarrie.)

14 cases (Fig. 59). It has been handed down through normal female carriers for at least six generations to VIII. 3. Number

V. 2 had frequent attacks of uncontrollable bleeding from nose and teeth, and was much crippled by joint hæmorrhages. His "two sons and grandson" were not hæmophilic, but according to the pedigree he had one son and a daughter. Again VI. 10 is stated to have had two sons and two daughters, all normal, yet the pedigree shows only two daughters. The descendants of normal males are all normal. VI. 12 is a case of a hæmophilic with children, his four sons all being normal as expected. Evidently in this family the bleeding is not so severe as in the Mampel family, but in female transmitters the coagulation-time and prothrombin-time were greatly prolonged. Of the 27 sons of transmitters in this pedigree, 14 are bleeders, 11 normal and 2 doubtful. Of the 12 women who have married, 10 have transmitted the disease. The next generation from VII. 11 should show whether VI. 10 has transmitted hæmophilia.

Davidson and McQuarrie also describe a sporadic case of hæmophilia with the characteristic blood picture. His ancestors and collaterals (65 individuals) showed no trace of the condition for four generations back.

Nissé (1927) considers all the evidence for transmission of hæmophilia by affected males and gives another pedigree, showing 6 cases in three generations. Examination of the 75 pedigrees of Bulloch and Fildes shows that only 47 out of 524 bleeders left offspring. In 12 cases there was transmission through daughters to their children, but most bleeders fail to reach adult life. In 3 instances there was apparent transmission through a normal male. But Pickering (1928) points out that these were not true hæmophilics. The speed of clotting was respectively 4½, 6½ and 9 minutes, and in one the count of platelets was only 87,000 per cu. mm. of blood. The condition was therefore not hæmophilia, but in one *thromocytopenia purpura* is indicated.

Lukowski (1927) gives a pedigree showing 8 cases of hæmophilia in five generations of a wealthy and intelligent Polish family (Posmiak), extending over a period of 132 years (1791-1922). In this family the condition takes an extreme form. All the hæmophilics died from slight accidents, and the gene is essentially a lethal. None of the women died of hæmorrhage, but many developed bluish marks from a slight bruise. The descendants from a sister of a bleeder show no bleeders through five generations. A baby, V. 23, born in 1922, was lightly slapped at birth to resuscitate him, causing large bluish marks lasting a week. At the age of four he bled

for forty-eight hours from a superficial chin wound, and at four he died after forty-four hours' hæmorrhage from a slight laceration of the rectal mucosa. A brother, V. 21, after many bleedings from slight wounds, died at the age of four from nosebleed caused by bumping his nose.

One more pedigree of hæmophilia will be given, as it involves several interesting features (Madlener, 1928). H. Dörr, who is number II. 6 in the pedigree (Fig. 60), had seven children and died in 1866, at the age of forty-six, of a clot on the brain. One of his daughters was a carrier, and another (III. 6) had subcutaneous hæmorrhages from an early age and often bled all day from a scratch. She became very pale from bleeding. Frau Dörr, her mother, had no known bleeders

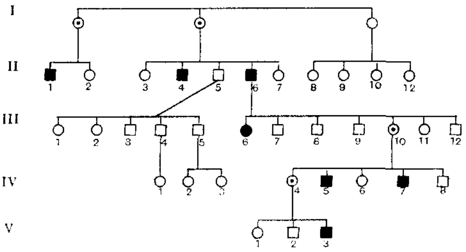


Fig. 60.—Pedigree of Hæmophilia. (After Madlener.)

in her pedigree or relatives (48 individuals included). This would appear to be a case of reversed dominance in the female. II. 1, 4 and 6 were also red-green colour-blind, this condition being inherited like hæmophilia. In this pedigree none of the female carriers showed longer clotting-time, so that the condition in III. 6 is all the more striking. The women III. 10, IV. 4, IV. 6 and V. 1 all belonged to blood group A. Lenz suggests that the case of III. 6 was perhaps one of pseudohermaphroditismus masculinus, an intersex.

As already hinted, there are many forms of bleeding which are not true hæmophilia, and these variable conditions are very difficult to classify. Hess (1916) and others have shown that the coagulation-time varies not merely in different families, but even in the same individual. The coagulation may be-

come normal for a time without other changes in the patient. The platelet count is found to be valuable in distinguishing between hæmophilia and purpura. In hæmophilia there is a normal count of platelets—*i.e.*, 200,000-400,000 per cu. mm., or it may even be above normal.

Hereditary nose-bleed (*epistaxis*) is recorded by Lane (1916), members of a family in Maine showing the trait through three generations. It is not, like hæmophilia, sex-linked. It manifests itself by spontaneous bleeding at the nose almost daily, beginning at the period of adolescence and continuing until eighteen or twenty. Individuals showing it are vigorous in health and grow rapidly, often feeling discomfort if the bleeding does not take place.

Pickering (1928) classifies the tendency to bleed abnormally as follows: (1) Hæmophilia, or bleeding from wounds, due to delay in coagulation: (2) *purpura hæmorrhagica*, multiple hæmorrhages visible as ecchymoses or livid spots on the skin from extravasated blood, but with normal clotting-time. In purpura, of which there are various forms, the hæmorrhages are spontaneous, there is a shortage of blood platelets, and they deviate from normal in size and shape, giant platelets commonly occurring. The capillaries are also easily ruptured. A series of other blood conditions related to these are classified, but little is known of their inheritance. He found that in mothers (carriers) of mild hæmophilia the clotting-time of the blood remained normal over a period of three years, while in the mother of a severe hæmophilic the time varied from 6 to 11 minutes. But such variations also occur in the blood of normal families. In the blood of hæmophilics, all the recognised participants in clotting appear to be present in normal amount. Hæmophilic blood, like that of lower vertebrates and of embryos, remains stable at room temperature, but is clotted at a temperature of 30° to 45° C. Pickering and Gladstone (1924) therefore suggest that hæmophilic blood represents an embryonic condition of the blood—a failure to complete development.

Among related conditions, Giffen (1927) describes four pedigrees showing hæmorrhagic disease only in the female line, the symptoms including epistaxis, hæmoptysis, and menorrhagia. There were fewer platelets in all cases. Libman and Ottenberg (1923) describe cases of hereditary hæmoptysis, Tidv (1926) cases of hereditary purpuras, and Glanzmann (1925) nine families in which the platelets were not reduced but

showed malformations. In an earlier paper Glanzmann (1918) describes a pedigree of *hæmorrhagic thrombasthenia*, with 10 cases in three generations, showing fewer platelets and less fibrin formation. The condition is not sex-linked and is an ordinary dominant, but a normal mother may transmit it to her children. Hess (1916) gives two families with hæmorrhagic disorders. In one family two males had hæmophilia and a female cousin was a purpuric type of bleeder, having epistaxis almost daily for a year at the age of eight. In the other family a brother showed hæmophilia and a sister purpura hæmorrhagica. The ætiology and inheritance of these and related conditions needs to be much more carefully studied.

Hæmorrhagic telangiectasis occurs in both sexes. This condition was first clearly outlined by Osler in 1901, who recognised its inheritance. Bleeding is generally spontaneous, from the nose in early life, followed by the development of red spider-markings in the skin. According to Tidy (1926) these are probably due to abnormal permeability of the endothelium of the small bloodvessels. Some 200 cases have been collected, and sometimes followed through four or five generations. Williams (1926) refers to 32 known cases and added several of his own, with dominant inheritance indicated. In Mekie's (1927) pedigree the condition is essentially the same and is evidently a dominant in inberitance. The onset of the disease is always at about fifteen years of age, with the appearance of these red spots at puberty, especially distributed about the nasal and buccal cavities. This condition, accompanied by recurrent hæmaturia, is described by Foggie (1928), who gives a pedigree in five generations showing it to be a simple dominant. East (1926) gives two pedigrees of *multiple facial telangiectases* due to a congenital vascular abnormality. There are 11 cases in three generations of one family, and 15 in three generations of another. The inheritance is that of a simple dominant, but in one family the parents of the three affected generations were both normal. In some members the lesions are slight and scarcely noticeable, in others they cause much trouble and discomfort.

Gutmann (1927) describes a remarkable pedigree of death by *apoplexy*. In five generations of a family of 38 persons, 15 of them have died of apoplexy, 5 more have long had heart disease and obesity, and 2 others committed suicide. Again, in three closely related families in a small town in Württemberg,

since the middle of the eighteenth century 82 members have died of apoplexy, chiefly heart-throb.

Curtius (1928) gives a short account of *phlebectasis*, or abnormal dilation of the veins, as an inherited dominant. Simple and varicose phlebectasis are recognised. The varicosis is regarded as only a partial effect of general mesenchyme weakness. Statistical correlations indicate a genetic relation between varicosis and hernia. Probably the genotypic substratum is a gene for "mesenchyme weakness," which varies much in its expression. About 1,200 cases were investigated.

The inheritance of a serious tendency to the *breaking of blood-vessels*, especially in the cavum nasi, is known in horses (Robertson, 1913). In the English thoroughbred racehorse there is a recessive gene which produces this result when present in the homozygous condition. The blood-coagulation is normal, but the bloodvessel walls must be fragile. The earliest known homozygous bleeder (not hæmophilic) is the stallion Herod, born in 1748. The next famous racehorse "bleeder" was Hermit, who won the Derby in 1867, and was descended on both sides from Herod. Similarly Gallinule, born in 1884, was descended from Hermit. These all left numerous progeny. Humorist, who won the Derby in 1921, died seventeen days later from bleeding. Robertson found in the records 185 horses who were "bleeders," and 17 died from it. The recessive gene which is responsible for this condition must be widespread in racehorse stock, and must be considered as a semi-lethal in the homozygous state.

Among many inherited peculiarities of the bloodvessels may be mentioned one cited by Windle (1891) from the *Chicago Med. Journ. and Exam.*, 1879, p. 475. The radial artery of a male in both arms passed over the supinator longus muscle at three to four cm. above the wrist, and ran over the radial extensors above the styloid process to its normal distribution. All his children had the same abnormality on the left side, and the daughters transmitted it better than the sons. Amongst the grandchildren it occurred in four on both sides, in four on one side, and was absent in seven.

Libman and Ottenberg (1923) describe a new form of hereditary bleeding from the lungs—*hæmoptysis*. The pedigree includes seven persons with the same histories of repeated profuse bleeding from the lungs, beginning at puberty and continuing at intervals through life. Tuberculosis was suspected, but there was no tuberculosis in the whole family.

The coagulation time was normal; the condition is not sex-linked and is not fatal. The health is not seriously impaired, and the inheritance is apparently that of a simple dominant.

Sickle-cell anæmia is a comparatively rare condition (Huck, 1923) in negroes and mulattoes. When the blood is examined *in vitro* the red corpuscles are seen to be sickle-shaped. Symptoms may be mild, severe, or absent, some quite normal individuals showing it when their blood is examined. The inheritance is that of a simple dominant, with 13 cases in three generations. The condition is more fully described by Taliaferro and Huck (1923). Some forms of pernicious anæmia have been regarded as due to a dominant Mendelian factor, but some are of course acquired. It has recently been looked upon (Piney, 1927) as a rudimentary condition or failure of development. MacLachlan and Kline (1926) describe the occurrence of 17 cases of anæmia in four generations, usually causing death, 13 having already died of it. The inheritance is again dominant.

Koltzoff (1924) first recognised inherited differences in the chemical properties of the blood. He found four types in guinea-pigs, according to the catalase content, also in fowls, cattle, and man. Later (1927) several thousand animals were tested to determine the catalase content of the blood. In guinea-pigs the resulting groups were, I.=0-3, II.=3-8, III.*a*=8-16, III.*b*=12-23. These types showed Mendelian segregation explainable by the formulæ I.=aaBb, II.=AAbb or Aabb, III.*a*=AABb or AaBb, III*b*.=AABB or AaBB.

In fowls, the catalase in the blood was found to be low, 0-2·3. The lowest catalase content (CC) was found in Orpingtons, Faverols, and Kochin Chinas. The highest (cc) was in Orloffs and fighting-cocks. All three conditions (CC, Cc, and cc) were present in Minorcas and Wyandottes.

In cattle, the index varies from 3 to 15, corresponding with the three higher genotypes of the guinea-pigs, while sheep all have a low index, 0·5 to 5·0, and probably form a single group analogous to AAbb of guinea-pigs. In man, in every case the index can fluctuate between 10 and 20, so a single group is supposed to be present, corresponding to AABB of guinea-pigs.

Koltzoff (1928) finds that races of guinea-pigs with low catalase are less resistant. Swiss, Dutch, and Jaroslav breeds of cattle have different mean indices.

LITERATURE

BAUER, K. H., and WEHEFRITZ, E. 1924. Gibt es eine Hämophilie beim Weibe? *Arch. f. Gynaekol.*, cxxi. 462-501.

BERNSTEIN, F. 1925. Zusammende Betrachtungen über die erbliche Blutstrukturen des Menschen. *Zeits. f. Abst. u. Vererb.*, xxxvii. 236-270.

CURTIUS, F. 1928. Die Vererbung der menschlichen Phlebektasien. *Verh. V. Internat. Kongr. Vererb.*, i. 576-577.

DAVIDSON, E. C., and MCQUARRIE, I. 1925. Hæmophilia: a study of the blood, the clinical course and the heredity of three cases. *Johns Hopkins Hosp. Bull.*, xxxvi. 343-356.

EAST, C. F. T. 1926. Familial telangiectasia. *Lancet*, ccx. 332-334.

FOGGIE, W. E. 1928. Hereditary hæmorrhagic telangiectasia with recurring hæmaturia. *Edin. Med. Journ.*, xxxv. 281-290.

GIFFEN, H. Z. 1927. Familial epistaxis without telangiectasia. *Amer. Journ. Med. Sci.*, clxxiv. 690-695, figs. 4.

GLANZMANN, E. 1918. Hereditäre hämorrhagische Thrombasthenie. Ein Beitrag zur Pathologie der Blutplättchen. *Jahrb. f. Kinderheilk.*, lxxxviii. 1-42, 113-141, pls. 3.

GUTMANN, M. J. 1927. Zum familiären Vorkommen des Schlaganfalls. *Arch. f. Rass.- u. Gesells.-Biol.*, xx. 70-71.

HESS, A. F. 1916. The blood and the bloodvessels in hæmophilia and other hæmorrhagic diseases. *Arch. of Int. Med.*, xvii. 203-220.

HUCK, J. G. 1923. Sickle cell anæmia. *Bull. Johns Hopkins Hosp.*, xxxiv. 335-344, pls. 4.

KLUG, W. J. 1926. Über die Kirchheimer Bluterfamilien (Mampel) *Deutsch. Zeits. f. Chirurgie*, cxcix. 145-151, pedigrees 2.

KOLTZOFF, N. K. 1924. Experimental biology and the work of the Moscow Institute. *Science*, lix. 497-502.

KOLTZOFF, N. K. 1927. Der Katalase-Gehalt im Blute als erbliches Merkmal. (Russian, German summary). *Journ. Exp. Biol. and Med. Moscow*, 303-334, figs. 11.

KOLTZOFF, N. K. 1928. Über erbliche chemische Bestandteile des Blutes. *Verh. V. Internat. Kongr. Vererb.*, ii. 931-935.

KOLTZOFF, N. K., and ELISAROVA, S. S. 1925. Über den Gehalt der Katalase im Blute von Meeresschweinchen (Russian with German summary). *Bull. Soc. Natur. Moscow, Sect. Biol. Exp.*, i. 82-107.

LANE, W. C. 1916. Hereditary nose-bleed. *Journ. Hered.*, vii. 132-134, fig. 1.

LENZ, FRITZ. 1912. Über die krankhaften Erbanlagen des Mannes und die Bestimmung des Geschlechts beim Menschen. Jena: Fischer, pp. 170, figs. 23.

LIBMAN, E., and OTTENBERG, R. 1923. Hereditary hæmoptysis. *Journ. Amer. Med. Assoc.*, lxxxi. 2030-2031.

LLOYD, BESS. 1925. Inheritance of hæmophilia. *Journ. Hered.*, xvi. 28-30, figs. 2.

LUKOWSKI, L. 1927. Five generations of hæmophilia. A supplement to the knowledge of hereditary tendency to bleeding. *Journ. Hered.*, xviii. 212-214.

MACLACHLAN, W. W. G., and KLINE, F. M. 1926. The occurrence of anæmia in four generations. *Amer. Journ. Med. Sci.*, clxxii. 533-543.

MADLENER, M. 1928. Eine Bluterfamilie. *Arch. f. Rass. u. Gesells.-Biol.*, xx. 390-394, figs. 2.

MEKIE, E. C. 1927. Hereditary hæmorrhagic telangiectasia. *Brit. Med. Journ.*, i. 423.

MOHR, O. L. 1926. Über Letalfaktoren mit Berücksichtigung ihres Verhaltens bei Haustieren und beim Menschen. *Zeits. f. ind. Abst. u. Vererb.*, xli. 59-109, pl. 1, figs. 10.

NISSÉ, B. S. 1927. The evidence of transmission of hæmophilia through the male with a new hæmophilic pedigree. *Ann. of Eugenics*, ii. 25-40.

PICKERING, J. W. 1928. The blood plasma in health and disease London : Heinemann, pp. 247.

PICKERING, J. W., and GLADSTONE, R. J. 1924. The coagulability of hæmophilic blood. *Journ. Physiol.*, lix. lxv-lxvi.

PINEY, A. 1927. Recent advances in hæmatology. London : Churchill, pp. 276.

ROBERTSON, J. B. 1913. The heredity of bloodvessel breaking in the thoroughbred. *The Bloodstock Breeders' Rev.*, ii. 265-281.

ROLLESTON, SIR HUMPHRY. 1928. The hereditary factor in some diseases of the hæmopoietic system. *Bull. Johns Hopkins Hosp.*, xliii. 61-80.

SCHLOESSMANN, H. 1924-5. Die Hämophilie in Württemberg, genealogische, erbbiologische und klinische Untersuchungen an 24 Bluterfamilien. *Arch. f. Rass. u. Gesells.-Biol.*, xvi. 29-53, 129-161, 276-303, 353-377.

TALIAFERO, W. H., and HUCK, J. G. 1923. The inheritance of sickle-cell anæmia in man. *Genetics*, viii. 594-598.

TIDY, H. L. 1926. On the hæmorrhagic diathesis : angio-staxis. *Lancet*, ii. 365-369.

WARDE, MILDRED. 1923. Hæmophilia in the female. *Brit. Med. Journ.* 599-600.

WEINBERG, W. 1924. Zur Frage der Letalfaktoren beim Menschen. *Zeits. f. ind. Abst. u. Vererb.*, xxxiv. 139-140.

WEINBERG, W. 1925. *Arch. f. Rass. u. Gesells.-Biol.*

WILLIAMS, C. M. 1926. Hereditary hæmorrhagic telangiectasia. *Arch. Derm. and Syph.*, xiv. 1-3.

WINDLE, B. C. A. 1891. Teratological evidence as to the heredity of acquired conditions. *Journ. Linn. Soc. Zool.*, xxiii. 448-502.

CHAPTER XI

METABOLIC DEFECTS AND DERANGEMENTS

In all cases of inborn deranged metabolism the probable cause is the lack of an enzyme, in the absence of which a chemical step is missed and some normal metabolic change fails to take place. All these cases are extremely rare, and Sir A. Garrod (1923) has summarised our knowledge of their nature and their inheritance. He includes under this head albinism (*q.v.*), alcaptonuria, cystinuria (and diaminuria), porphyrinuria, hæmatoporphyria, steatorrhœa, and pentosuria. They are all inherited as recessive conditions, usually in sibs with normal parents, and as they marry normals, their children are usually immune. They are, however, much commoner in men than women, but temporary alcaptonuria occurs in women, and toxic porphyrinuria due to sulphonal is almost confined to women.

Cystinuria is the least rare of the six. Simon found one case of cystin sediment in examining the urine of 15,000. Primavera found one case in 20,000. The condition is also known in dogs. It has been described in three generations of more than one pedigree. A cystinuric mother and a normal father had twelve children, and seven of ten examined excreted cystin. Two normal parents who were first cousins had four children, all cystinuric. In another family, two normal and unrelated parents had three children, all with cystinuria. From these and similar cases there are probably, as Punnett suggests, two independent factors, which must both be present to produce cystinuria. Robson (1929) has recently studied the protein metabolism in a family of cystinurics with 12 cases in three generations. They all trace their ancestry to common great-grandparents, the third generation including three families from intermarriages. Although the pedigree is incomplete, it is in accord with a two-factor hypothesis.

In Europe and America 120 cases of alcaptonuria have been recorded. Bateson, in 1902, suggested that it is a Mendelian recessive, and this has been confirmed by the later evidence. The condition is characterised by the presence of alcaptan

(probably a derivative of tyrosin) in the urine, and results from the absence of an enzyme. The amino acids, phenylalanin and tyrosin, are then not completely destroyed in the body, and they colour the urine, also causing arthritis and the deposition of pigment in the cartilages. Charts compiled by Toenniessen (1922) show three unaffected children to one affected (23 normal : 8 affected, in three sibships). Also in one mating RR × DR there were four with alcaptonuria and four without it. The condition is not sex-linked.

PENTOSURIA (in which pentose sugar is found in the urine) is a chemical anomaly to which Jews appear to be specially liable. Records from various families suggest that the inheritance is the same as for cystinuria. Forty-four cases are recorded. Garrod gives one pedigree in three generations, and another with affected sibs from normal parents. Different metabolic anomalies may be included under this term.

Regarding HÆMATOPORPHYRIA, 18 cases are on record, but the evidence is insufficient to judge the method of inheritance. Only three cases of STEATORRHŒA are known. This is not, like the others, an error in protein metabolism, but is concerned with the utilisation of fats. It is apparently due to a deficiency of the pancreatic secretion. The first case was described in 1911. Two brothers occurred in a family of five children from a marriage between cousins. Another boy occurred in a family of three whose parents were unrelated. The evidence, so far as it goes, suggests a recessive character. One boy grew up in active work and adjusted his diet so that " butter stools " were seldom passed. The waste of fat is less than that caused by disease of the pancreas.

Related to these is HYPERGLYCEMIA, which has been described as a recessive Mendelian character in mice (Cammidge and Howard, 1926). The sugar content of the blood in a strain of mice was found to vary. Breeding experiments showed that high sugar content (about 120 mg.) is recessive to normal (about 80 mg.). When a heterozygous normal is bred to a mouse with high sugar content, the offspring show equal numbers of the two types. This condition was independent of coat colour.

Conditions bearing certain similarities although not metabolic in causation may be referred to here, namely HÆMATURIA, ALBUMINURIA, and related conditions.

Dickenson (1875, i. 379) gives a pedigree of a condition called albuminuria, showing 11 cases in three generations, the

inheritance evidently being that of a dominant. Portraits of ancestors of this family as far back as the Wars of the Roses show a characteristic clear, transparent pallor like modern members, indicating that the condition has been transmitted from that early time.

Guthrie (1902) published a pedigree of hæmaturia showing its inheritance (as a Mendelian dominant), with 12 cases in three generations. The condition in this family was not postural, could occur by day or night, and was regarded as representing a congenital weakness or varicosity of the walls of the renal vessels. Hurst (1923) regards hæmorrhagic nephritis as a better term for this condition than hæmaturia, because often only traces of blood were present in the urine, while there was much albuminuria, the hæmaturia being intermittent, but albumen present between the attacks. He published a pedigree (Fig. 61), with 16 cases in three generations. The

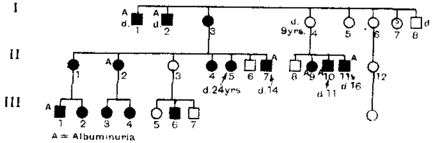


FIG. 61.—PEDIGREE OF HÆMORRHAGIC NEPHRITIS. (After A. F. Hurst.)

inheritance is clearly dominant. Individuals with albuminuria are marked A. Number II. 3 had epistaxis and hæmatemesis. There is some irregularity of the dominance in this pedigree, two females skipping a generation. The condition was more severe in some, slight in others, but it evidently increased from youth to adulthood. Hæmaturia can be brought on by eating strawberries or asparagus, and in several women, but not in a man, by black currants or claret. Hurst also cites Benson's case with four individuals in a family having acute nephritis developed from œdema and albuminuria; Atlee's case of three sisters with albuminuria and intermittent hæmaturia, the father dying of uræmia; and Fergusson's case in which father, mother, and eight children all had albuminuria.

DIABETES MELLITUS is a chronic disturbance of the metabolism, manifesting itself especially by increase in blood sugar (hyperglycæmia) and by excretion of sugar in the urine (glycosuria).

It causes emaciation, loss of strength, thirst, and polyuria, and finally diabetic coma. A diabetic patient's life may be maintained indefinitely by feeding insulin, the condition being primarily due to a deficiency of this secretion from the pancreas. The manner of inheritance of this condition is at present uncertain and may vary in different families. Meulengracht (1925) holds that diabetes mellitus is due to a single dominant factor, and Hausen (1924) concluded it was due to several factors having similar effects, according to the mildness or severity of the disease.

ORTHOGLYCÆMIC GLYCOSURIA, or "leaky kidneys," is a benign condition which does not progress to diabetes mellitus. Hjärne (1927) investigated a family of good social position in Sweden and Finland having this condition. Six generations were descended from a single pair, the last three generations being examined. Among 199 persons, 18 (in perfect health) had orthoglycæmic glycosuria, 19 had glycosuria without diabetic symptoms, 7 had diabetes mellitus, and 2 others were aberrant. Normal parents without glycosuria had in 13 cases only normal children (44). Orthoglycæmic glycosuria was present in younger persons of both sexes and was inherited as a monofactorial dominant. The diabetes in the pedigree was an independent unrelated condition. When the father had orthoglycæmic glycosuria and the mother was diabetic there was no summation of effects in the children. Holst (1926) describes eight families in which both diabetes mellitus and glycosuria occurred. These cases of glycosuria were of no definite type, but included cases due to alimentary hyperglycæmia as well as the renal form. He concludes that there must be a hereditary relation between diabetes and the nondiabetic glycosuria. The nature of this relationship is uncertain, but it is probably not entirely due to a quantitative difference.

Gossage (1908) describes Weil's pedigree of DIABETES INSIPIDUS, or polyuria, which was a simple dominant in inheritance, with 23 cases in five generations. In eight sibships from DR × RR there were 23 affected to 26 normal. In this disease the patient develops excessive thirst and drinks large quantities of water, but may live to old age. The condition may be either congenital and inherited or acquired and non-inherited—*i.e.*, it may result from an inherited germinal change or from an impressed modification. In Weil's case, also cited by Bulloch (1909), the original progenitor was born in 1772 in Oberhessen

and had 220 descendants in four generations, 34 of whom had diabetes insipidus. A generation is skipped but once. Chase (1927) gives another pedigree in five generations showing inheritance as a Mendelian dominant. One man in this family would drink a pail of water without taking it from his lips. He lived to eight-five years of age.

JAUNDICE may be included here. It is, of course, sometimes produced by an injury or other condition which occludes the bile duct, and so produces the characteristic yellow colour of the skin. But there are also hereditary forms of the disease. Claude Wilson, in 1890, published an account of 6 cases in three generations of a family, calling it " hereditary enlargement of the spleen." Minkowski, in 1900, in a review of the subject published an account of 8 cases in a family which showed enlarged spleen, jaundice with bile absent from the urine but present in the stool, and excess of urobilin in the urine. The condition is now known as congenital family jaundice or acholuric jaundice. Meulengracht (1922), in a monograph on this rare disease, collected 50 cases occurring since 1914. He gave a good account of 8 families having 33 cases of acholuric jaundice, behaving as a dominant factor. In one case apparently the condition had arisen *de novo*. Twelve underwent splenectomy with good results. Campbell and Warner (1926) describe 15 cases in a family in five generations. They formerly concluded that it was not a dominant because an apparently normal parent had in two cases children which showed the symptoms. When the blood of these individuals was examined, however, it showed the characteristic changes of acholuric jaundice—*i.e.*, diminished resistance of the red corpuscles to hæmolysis by sodium chloride. The blood also contained bile and the urine an abnormal amount of urobilin. Hence Campbell and Warner agree with Meulengracht that the inheritance is that of a dominant, although some affected individuals may not show all the symptoms.

Manson (1928) describes a pedigree of hereditary icterus in which there is no splenic enlargement and the length of life is not affected. The skin and conjunctiva are yellow, but there is no bile in the urine. Six cases were observed in four generations, in which the yellowing of the skin was found to be due to an increase of bilirubin in the blood and a loss of red corpuscles. A brother of an affected member had a normal appearance, but his blood contained five times the normal amount of bilirubin. In affected individuals the

bilirubin content was 17 to 30 times the normal. They have a characteristically cheerful, placid temperament. Doll (1926) also points out that hæmolytic icterus can occur with or without jaundice symptoms, in the same pedigree or even at different times in the same person.

Writers usually classify GOITRE as endemic or sporadic. Exophthalmic goitre appears to be the result not merely of an increased secretion of the thyroid hormone but also of a slightly deranged hormone. Goitrous enlargement of the thyroid is particularly characteristic of certain regions, such as certain parts of Germany and Switzerland. It is frequently attributed to a deficiency of iodine in the soil or the drinking water, and there has been an attempt to show that the disease is concerned

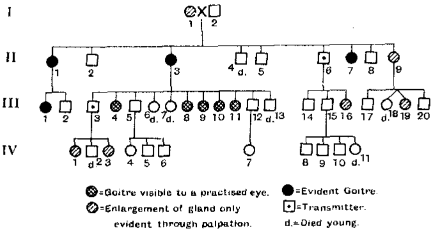


FIG. 62.—PEDIGREE OF GOITRE. (After Bluhm.)

with a specific bacillus, one host of which is the goat and which may be conveyed by contamination of drinking water. But all these explanations remain uncertain.

There is no doubt that goitre is more frequent in some regions than others, but on the other hand it is clear from various pedigrees that there is an inherited constitutional element involved. The disease is much commoner in women than in men. Riebold (1915) collected 65 cases of goitre, 78 per cent. of which were in females. He concludes from the study of nine pedigrees that goitre is inherited as a Mendelian character, dominant in females and recessive in males. But his pedigrees show cases where a male who must be heterozygous has the disease. Hence there would be variable dominance in the male.

Fig. 62 is from one of Bluhm's (1922) pedigrees, showing

transmission by unaffected males in two cases. The father of I. 1 belonged to a Dutch family and lived in Heidelberg, on the edge of a goitre region, until twenty-two years of age. I. 1 married an officer in Westphalia and lived there in a region free from goitre. The daughter, II. 1, married an East Prussian officer. She had a goitre as large as a child's head, and lived in Berlin in her old age, dying at ninety. Her daughter, III. 1, also lived in goitre-free East Prussia until thirty, but developed the disease. The original progenitors of this pedigree had 20 female descendants in three generations. Four of these had obvious goitre, in five more it was apparent to a trained observer, and five had it only in a slight degree. The remaining six died in infancy or too young to show it. In this pedigree only females show the disease, and its onset is not before middle life. There is no satisfactory hypothesis to explain its mode of inheritance. Under the circumstances, the compilation of many careful pedigrees with full details of the life-history will be necessary before its inheritance can be understood. Theoretically, goitre may be confined to one sex (sex-limited), or the male sex may have a goitre-suppressing effect. Siemens (1917) criticises Riebold's conclusions, contending that goitre is not a single illness but a symptom, and the diseases causing it may be very different in their ætiology. Some forms of so-called sporadic goitre are genotypically determined and hereditary. But the method of inheritance remains doubtful. Siemens gives a pedigree of a woman born in 1790. In each of the three following generations one woman had it, in the fourth generation two. Hence, although it appears to be sporadic, it is really hereditary in this family. In another pedigree a normal mother had a goitrous son, and in three a goitrous father had a normal daughter. Siemens (1923) gives a pedigree of so-called sporadic goitre, with 9 cases in six generations, living in a non-goitrous region. It is confined to females and inherited directly from mother to daughter. In another pedigree, of endemic goitre, all the grandparents were normal, the parents were both affected, and their five children, all sons, were affected.

LITERATURE

Bluhm, Agnes. 1922. Zur Erblichkeitsfrage des Kropfes. *Arch. f. Rass. u. Gesell. Biol.*, xiv. 1-9.

Bulloch, W. 1909. Diabetes insipidus. *Treas. Human Inheritance*, pt. i., 1-6, pl. 1.

CAMMIDGE, P. J., and HOWARD, H. A. H. 1926. Hyperglycæmia as a Mendelian recessive character in mice. *Journ. Genetics*, xvi. 387-392.

CAMPBELL, J. M. H., and WARNER, E. C. 1926. Heredity in acholuric jaundice. *Quart. Journ. Med.*, xix. 333-355, figs. 2.

CHASE, L. A. 1927. Hereditary diabetes insipidus. *Canadian Med. Assn. Journ.*, xvii. 212-214, figs. 3.

DICKENSON, W. H. 1875. *Diseases of the Kidney.*

DOLL. 1926. Über familiären hämolytischen Ikterus (familiäre hämolytische Anämie). *Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, xl. 12-33.

GARROD, SIR ARCHIBALD E. 1923. Inborn errors of metabolism. 2nd edition. Hodder and Stoughton, pp. 216.

GOSSAGE, A. M. 1908. The inheritance of certain human abnormalities. *Quart. Journ. Med.*, i. 331-347.

GUTHRIE, L. G. 1902. "Idiopathic" or congenital hereditary and family hæmaturia. *Lancet*, i. 1243-1246.

HJÄRNE, URBAN. 1927. A study of orthoglycæmic glycosuria with particular reference to its hereditability. Stockholm: Norstedt and Sömer, pp. 149, figs. 3.

HOLST, J. E. 1926. The occurrence of benign glycosuria in diabetic families. *Arch. Int. Med.*, xxxviii. 279-291.

HURST, A. F. 1923. Hereditary familial congenital hæmorrhagic nephritis. *Guy's Hosp. Rep.*, lxxiii. 368-370.

MANSON, J. S. 1928. Observations on human heredity. London: Lewis, pp. 84, pls. 8, figs. 19.

MEULENGRACHT, E. 1922. Der chronische hereditäre hämolytische Ikterus. Leipzig: Klinkhardt, pp. vi + 226, pls. 5.

MEULENGRACHT, E. 1925.

RIEBOLD, G. 1915. Die Erblichkeit der Struma. *Zeits. f. Abst. u. Vererb.*, xiv. 1-11, figs. 9.

ROBSON, W. 1929. Protein metabolism in cystinuria. *Biochem. Journ.*, xxiii. 138-148, figs. 2.

SIEMENS, H. W. 1917. Die Erblichkeit des sporadischen Kropfes. *Zeits. f. Abst. u. Vererb.*, xviii. 65-80, figs. 4.

SIEMENS, H. W. 1923. Einfühung in die allgemeine und spezielle Vererbungspathologie des Menschen. Berlin: Springer, pp. 286.

TOENNIESSEN, E. 1922. Über die Vererbung der Alkaptonurie des Menschen. *Zeits. f. Abst. u. Vererb.*, xxix. 26-30.

CHAPTER XII

ALLERGIC DISEASES

ALLERGIC DISEASES, such as hay fever and other forms of hypersensitiveness, which exist in great variety, are undoubtedly inherited in many cases, although the symptoms are often variable and difficult to define, and the exact nature of the inheritance is often difficult to trace. Not only does specific sensitiveness to many kinds of food exist in different individuals, but many people are sensitive to the emanations from particular animals, such as horses, cats, and rabbits. Napoleon, Wellington, and Lord Roberts are all said to have been afflicted with "horror of cats." "Cat asthma" and "horse asthma" are conditions which may be induced in hypersensitive people by the presence of these animals or of hairs or other emanations from them. All of these conditions, sensitiveness to particular animals or foods, or to the pollen from particular plants, vary greatly in their specificity and depend apparently upon the presence of certain protein substances.

Drinkwater (1909) gives a pedigree showing the inheritance of spasmodic asthma as a simple dominant character, with 10 eases of its occurrence in three generations. In four sibships from DR × RR the offspring were ten asthmatic : nine normal.

Bronchial asthma and hay fever form a closely associated set of phenomena which are clearly inherited in families, and have their basis in hypersensitiveness to proteins and in the nervous system. Hay fever is a slight form of the condition, which may develop asthmatic symptoms under special irritation or lowered bodily vitality, and, as is well known, may appear or disappear in an apparently capricious manner at different ages or under different climatic conditions. A considerable study of asthma from the clinical and inheritance point of view has been made by Adkinson (1920). She studied 400 cases, and found a history of asthma in the family in 48 per cent. of the cases. Of the total, 191 were sensitive to protein as demonstrated by skin tests, while the remaining 209 were

negative to tests. There was a larger percentage of inherited asthma in the former group.

The latter type or "sensitive asthma" is more like intensified bronchitis. Both types "run in families," and both usually occur in different members of the same family. Asthma is found to be inherited with equal frequency through either parent. Thirty-eight family histories are presented, and the general conclusion to be drawn from these is that the asthmatic tendency is inherited as a Mendelian recessive. Considering individual cases, "from the father's family 66 patients may have inherited asthma, 39 directly, 8 skipping a generation, 1 skipping two generations, and 18 collaterally. From the mother's family, 64 patients may have inherited asthma, 25 directly, 22 skipping a generation, and 18 collaterally." It is found that "a nearly equal number of men and women inherit asthma from the father, but twice as many women as men inherit asthma from the mother, and 25 per cent. more women than men inherit asthma directly from the parents."

It is concluded (1) that where both parents have asthma or hay fever, all the children tend to show the condition. (2) Where one parent has asthma and one is normal (seventeen matings), all the children (sixty) are normal. (3) When one parent is asthmatic and one normal, but probably carrying the condition (simplex), then equal numbers of the offspring are affected or unaffected (sixty asthmatic and sixty-seven normal). (4) When both parents were normal, but could be shown or must be assumed to be carrying the condition (simplex), there were three times as many asthmatic as normal children. This is the reverse of expectation. It is partly explained by incomplete records of normals, and in part by the addition of the non-transmitting type of asthmatics. But it is at least possible that in a character of this kind, in the cross DR × DR the recessive character is able to express itself in some instances in the heterozygous condition.

Coca and Cooke suggest ATOPY as an inclusive term for inherited hypersensitiveness. Cooke and Vander Veer studied the inheritance in 504 cases of atopy. They comprised hay fever, bronchial asthma, urticaria, angioneurotic œdema and acute gastro-enteritis following the eating of fish or strawberries. They conclude that inheritance is involved. Cooke and Spain (1924) studied 568 cases of hay fever and asthma (each case being subjected to a skin test). From these, 54 cases are excluded on the grounds of insufficient evidence, and 52 from

lack of family evidence, leaving 462. Of these, 41 per cent. have a negative history. No pedigrees are given and the paper is unsatisfactory from this point of view, but indications are given of normal and affected sibs and relatives. They conclude, contrary to Adkinson, that the condition is not a simple recessive, because when both parents have it only 71 per cent. of the children show it. It appears probable from present knowledge that multiple recessive factors are concerned, more than one of which is necessary to produce the symptoms.

Cooke and Spain find a relation between time of onset of the symptoms and frequency of their occurrence in the ancestors. Thus in 53 per cent. of the families where both parental lines of ancestors include positive cases, the symptoms appear within the first five years of life and in 26 per cent. of families in the second to fifth years. When only one line of ancestors is afflicted, the symptoms appear later, 31 per cent. in the first ten years, 80 per cent. in the first thirty years. When there is a negative family history on both sides, then the appearance averages still later, only 12 per cent. in the first five years and 12 per cent. for each age group up to fifty-five years.

Phillips and Barrows (1922) discuss the inheritance of ANGIONEUROTIC ŒDEMA. Quincke in 1882 recognised the disease as hereditary. The symptoms are sudden swellings of the skin or mucous membrane persisting for a few hours or days and then suddenly disappearing. An individual may have it but once or with more or less frequency. Sometimes the attacks are periodic and the swellings enormous. The symptoms may appear in childhood or middle life, but are usually less annoying in old age. Œdema of the glottis causes death, and Crowder and Crowder (1917) give a pedigree (Fig. 63) with 28 cases in five generations, 15 of whom died of glottis œdema. Here the inheritance is clearly a simple Mendelian dominant with no exceptions. Œdema has been ascribed to nervous influences, infections, endocrine disorders and dietetic errors, but allergy—*i.e.*, hypersensitiveness to specific substances—is the most plausible explanation. Whether individuals are born so, or born with a tendency to become easily sensitised, is uncertain. The eating of certain foods causes the attack, but in some cases an attack can occur without it. There are two types—(1) prompt, (2) delayed. With the prompt type, the taking of a particular food is followed by nausea and later by urticaria and in some cases œdema. In the delayed type the

interval may be hours or days. When it occurs sporadically it is often associated with eczema, urticaria, hay fever, asthma, etc., in the family history. These diseases seem to differ mainly in the distribution of the hypersensitive tissues and the intensity of their reaction, and it is quite likely that susceptibility to them is inherited. There are many pedigrees of the familial type, and generally sibships from a normal and an affected parent give 1 : 1 ratios, indicating that angioneurotic œdema is a simple dominant. But whereas 27 matings between normal parents one of whose parents had been affected gave only normal children (81), yet in other matings (37 per cent.) one

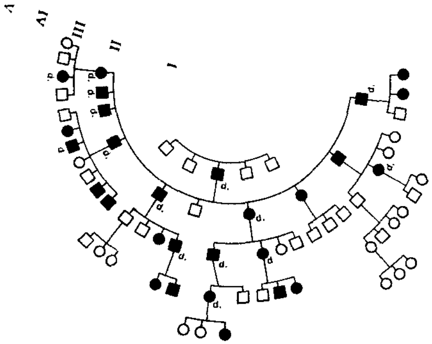


FIG. 63.—INHERITANCE OF ANGIONEUROTIC ŒDEMA. (After Crowder and Crowder.)

of the two normal parents must have transmitted the condition, since it appeared in the children. Thus again we have "variable dominance," which is so characteristic of many human pedigrees.

There are two possible explanations of these cases of skipping a generation. (1) Angioneurotic œdema is a fundamental condition which requires some stimulus to bring it out, that stimulus being the eating of a particular food. If an individual eschews that particular food he might never discover his sensitiveness to it and he would receive a negative mark in the pedigree. This could not apply, however, to common foods.

(2) The condition may be due, in some pedigrees, to two closely linked factors. If this is the case, each normal parent would carry one factor, and these on crossing over would tend to be inherited together as a dominant trait. One of these factors may be the same one that makes the bearer develop asthma, eczema, hay fever, or urticaria. The second factor might be like the first, but probably it would be different, producing the œdema. It is well known that these conditions all occur in the same pedigree, and the same person may be afflicted with asthma and œdema.

A pedigree of allergy (Fig. 64), with 36 cases in four generations, is given by Smith (1928). In this family asthma, hay

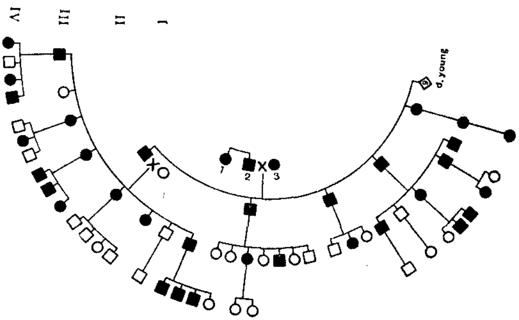


FIG. 64.—PEDIGREE OF ALLERGIC HYPERSENSITIVENESS. (After A. E. Smith.)

fever, vasomotor rhinitis, urticaria, angioneurotic œdema, and eczema all occur, but the same form of allergic manifestation tended to appear in the closely related groups within the pedigree. The parents of I. 2 were first cousins, and he married a first cousin of both his parents. Hence there was much inbreeding in the ancestry. This pedigree looks like a simple dominant if one does not distinguish between the different forms of allergy represented. But this is very doubtful when all is considered. Hypersensitiveness may be the result of combined independent factors. Smith concluded that it cannot be a simple dominant or recessive although so clearly inherited.

Balyeat (1928), in a discussion of the hereditary factor in allergic diseases, concludes that the atopic substance is not necessarily a protein, but is often non-nitrogenous. He finds that patients are born specifically sensitive, but that specific sensitivity is not inherited. All children do not show allergic conditions when the parents are both affected. Hence it cannot be a simple recessive. Balyeat concludes that general sensitiveness is inherited as a simple dominant, but some of his pedigrees would be equally in accord with a recessive factor. In one pedigree hay fever and asthma are interchangeable. In another, migraine and urticaria are interchangeable with asthma and hay fever. He thinks they all have a common cause, but this is very doubtful. Allergic patients have one advantage in that they develop a general resistance to infectious diseases which is far above normal. The earlier in life

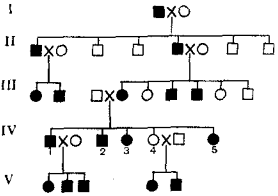


FIG. 65.—INHERITANCE OF RABBIT ASTHMA. (After Fantham.)

an individual becomes sensitive, the greater is the tendency to develop sensitivity to more than one group of proteins. Development of specific sensitiveness depends much on exposure to a particular protein. The thing which is inherited is the ability to become sensitive. From an examination of 40 allergic students, 70 per cent. were found by intelligence tests to be above the average in mentality.

Fetscher (1927) gives four pedigrees of HAY FEVER. He points out that the symptoms often appear after puberty, but also frequently occur before the fourteenth year. He concludes that it is probably recessive, but leaves open the question whether polymery (multiple factors) and sex-linkage or sex-linked factors play a rôle.

Fantham (1925) has compiled a striking pedigree of "RABBIT ASTHMA" (Fig. 65), with 17 cases in five generations,

from a family in Johannesburg. In those affected, the smell of rabbits or a piece of rabbit skin on a coat was sufficient to cause asthma, and illness was caused by eating rabbit. The condition appears to be a simple dominant, but one normal woman (IV. 4) transmits it to both children.

Some American families are found to be more markedly susceptible to poison ivy (*Rhus toxicodendron*) than others. McNair (1924) found that among 28,756 university students, 5·57 per cent. were treated for Rhus dermatitis. But this proves nothing, because large numbers of students would never be exposed to it. Crew (1928) has discussed the genetical aspects of natural immunity and resistance to disease, with various facts bearing on this subject.

LITERATURE

ADKINSON, JUNE. 1920. The behaviour of bronchial asthma as an inherited character. *Genetics*, v. 363-418, figs. 39.

BALYEAT, R. M. 1928. The hereditary factor in allergic diseases. *Amer. Journ. Med. Sci.*, clxxvi. 332-345.

COOKE, R. A., and SPAIN, W. 1924. Studies in specific hypersensitiveness. IX. The familial occurrence of hay-fever and bronchial asthma. *Journ. Immunol.*, ix. 521-569.

CREW, F. A. E. 1928. Genetical aspects of natural immunity and disease resistance. *Edin. Med. Journ.*, xxxv. 301-321, 383-404.

CROWDER and CROWDER. 1917.

DRINKWATER, H. 1909. Mendelian heredity in asthma. *Brit. Med. Journ.*, i. 88.

FANTHAM, H. B. 1925. Some factors in eugenics, together with notes on some South African cases. *S. African Journ. Sci.*, xxii. 400-424, figs. 4.

FETSCHER, R. 1927. Zur Vererbung des Heuschnupfens. *Arch. f. Rass. u. Gesells.-Biol.*, xix. 187-189.

McNAIR, J. B. 1924. Hereditary immunity to rhus dermatitis. *Med. Journ. and Record*, cxix., cxxix-cxxxi.

PHILLIPS, J. M., and BARROWS, W. M. 1922. Heredity of angioneurotic œdema based on a review of the literature. *Genetics*, vii. 573-582, figs. 5.

SMITH, A. E. 1928. Occurrence of hypersensitiveness or allergy in five generations of one family. *Arch. of Int. Med.*, xli. 472-481.

CHAPTER XIII

EARS, TEETH, AND TAILS

Ears.

Ears are a feature which has been relatively little studied from a genetic point of view. Dahlberg (1926) has made an extended record of ear-shapes, with photographs in twins, showing that many small details of conformation must be inherited. Lenz says that adherent earlobes is an hereditary anomaly often depending on a single unit. Hildén (1922) gives three good pedigrees of adherent earlobes, from Rüno Island off the coast of Riga. When both parents have it, all the children have it. When both parents are free, all the children are free or some adherent. Hence it is a simple monofactorial difference, with adherent earlobe recessive to free earlobe. Attached earlobe was formerly regarded as a stigma of criminality or insanity, but Hildén shows that there is no connection with any mental or physical abnormality. Carrière (1922) concluded that adherent earlobe is dominant, but he had not enough evidence to prove his case, and Hildén is probably right.

Much remains to be done on the genetics of ears. According to Bean (1925) human ears are decreasing in size and changing in shape. The ear undergoes retrograde metamorphosis before birth. Negroes have the smallest ears of any race—a case of reduction. The Asiatic yellow-brown races have the largest and least retrograde, the Kalmucks being credited with the largest ears of all. The ears of the white race are intermediate.

Various inherited abnormalities of the ear have been described, both in man and animals. Absence of the external ear is cited (Windle, 1891) in a case where a normal father had a son with the defect. The father's male cousin had the defect, and two of his male children, but a daughter was normal. A Mendelian dominant is suggested, a result which is especially interesting in the light of recent experiments with earless sheep, given below. Sedgwick (1861) cites a case of a boy with no

external left ear, the meatus being imperforate. This boy's father had a male cousin whose two sons exhibited a deficiency of the cartilage of the left ear, while the daughter was normal. The manner of inheritance is not clear, except that it is from the original great-grandparents, and it is confined to one side of the head. In another case a woman, two of her daughters, and two granddaughters had rudimentary lobules to their ears, the male children and grandchildren being normal. The rudimentary lobules probably represent the heterozygous condition, but there is not sufficient evidence of sex-linkage. Sedgwick (1863, p. 457) describes a line of descent in three generations with rudimentary earlobes adherent to the head. The condition appears to have occurred only in the women. It was present in the grandmother, in two of her daughters, the third not being examined, and one of the two sons examined being normal. One of the daughters who had the peculiarity transmitted it to her two daughters, the son being normal. No doubt many other ear peculiarities are inherited.

Hildén (1929) has made a study of Darwin's ear-point or tubercle in the population of Finland. In various people the infolded edge of the helix has a more or less conspicuous projecting point which Darwin (*Descent of Man*) regarded as a remnant of the erect, pointed ears of our anthropoid ancestors. Schwalbe recognised six stages in the condition, from the most extreme everted point (Macacus form) to its complete absence, and Keith showed the existence of a chain of intermediate forms. Hildén examined this point in the ears of the pupils in two Finnish and two Swedish schools in Helsingfors, numbering in all 2,077 children with 4,154 ears. Forty of these ears (less than 1 per cent.) belonged to the extreme Macacus form, 187 belonged to form three, with a typical inturned point or tubercle, and in 2,215 ears there was no trace of the tubercle. Darwin's tubercle in one of its five forms was present in 50 per cent. of the boys and 43 per cent. of the girls. This excess of the more primitive ear form in boys was chiefly due to the Swedish boys, there being only a slight excess of frequency in Finnish boys. Darwin quotes Meyer as also recording the tubercle more frequently in men than in women.

When present in only one ear, Darwin's tubercle was rather surprisingly found to be twice as frequent in the right as in the left, the greater reduction of this condition in the left ear applying consistently to both the boys and the girls of each race independently. It was also found that the five types of Darwin

tubercle were consistently more frequent in Swedish than in Finnish children. This difference is ascribed to the different proportions of the East Baltic and Nordic races in the two peoples.

Lynch (1921) describes a mutation in the house-mouse, in which the ears are about half the normal length and somewhat narrower. They also differ somewhat from the normal in outline, and are held close to the head. The character behaves as a simple Mendelian recessive.

Ritzman (1921) has found that short, thick ears in a breed of sheep is a heterozygous condition, giving equal numbers of both types of offspring in crosses with the normal (sixteen short ear : sixteen long ear). The mating together of short-eared individuals has produced an earless ram, which therefore clearly represents the pure recessive condition. Similar results have been independently obtained in Norway by Wriedt (1919, 1921, 1925), who adds that an earless ram mated with normal sheep gave five offspring with short ears, while an earless sheep mated with a normal ram produced one lamb with short ears. Short ear × short ear gave 2 short : 2 earless, and earless individuals mated together gave earless offspring. A simple Mendelian pair is evolved, with short ear as the heterozygous condition. Short ears in sheep were said to be very common formerly in Norway, and are still found in many parts of the country. There is evidence that both the short-eared and earless conditions are found also in the Karakul breed of Bokhara.

Hopf (1909), who records many developmental abnormalities in man and animals, describes a litter of rabbits which contained one with a single ear. From this a race of one-eared rabbits was produced.

Yamane (1915) described the inheritance of "notched ears" in Ayrshire cattle. The full notch is dominant, the heterozygous condition being usually slightly notched.

Lush (1922) described the same notch in the ear in Jersey cattle. This character was found in a Jersey bull at the Texas Agricultural Experiment Station, and is inherited as a simple dominant, the bull (Gamboge's Raleigh) being heterozygous. Thirty of his calves were examined and twelve found to be without the notch. There is much variation in the degree of expression of the notch.

"Double ears" is an apparently dominant character, found in Brahma cattle (Lush, 1924). It is the name given to

a condition in which a piece of cartilage projects out at the back of the ear. Some of the calves descended from a certain bull with double ears showed the condition, and some of their descendants showed it in crosses with normal cows.

As an example of the inheritance of a slight peculiarity may be cited the case of a bilobed ear described by Schofield (1917). In this family the condition has been transmitted through four generations, only the right ear having the peculiarity. The accompanying chart (Fig. 66) shows its incidence.

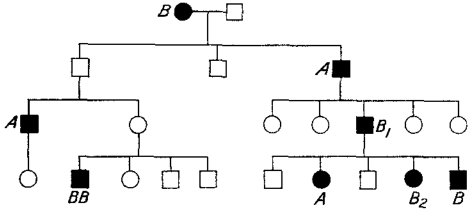


FIG. 66.—PEDIGREE CHART SHOWING INHERITANCE OF RIGHT BILOBED EAR.

One generation or even two may be skipped, and the condition varies considerably in different individuals. Thus, in A there is a very marked deep cleft of considerable length, while in those marked B the cleft is not so well marked. In BB it was only a furrow, while in B_1 and B_2 there is a deficiency of hearing in the bilobed ear. The family with pitted ear-lobes, described by Jenks (1916), is a similar case.

Kindred (1922) gives the pedigree of another family, in which a peculiar little pit occurs in the skin at the proximal end of the upper part of the helix of the left ear. This is known to have occurred in four generations, as is shown by the chart (Fig. 67).

The propositus (III. 7) has the pit, as well as her father and father's father. Some of her father's brothers and sisters probably had the mark, because some of her cousins were known to have it. Three of her sisters who married all had one or more children showing the mark, although two of them did not have the pit themselves. One of the most remarkable features of these slight peculiarities is their unilateral occurrence, being confined to the right side in one family and the left in another.

We are at present at a loss to picture the hereditary mechanism by which this comes about.

A case is cited (Jenks, 1916), with some evidence of authenticity, in which a girl of Swedish ancestry, whose ancestors of both sexes had been accustomed for many generations to wear earrings, was born with a hole in the proper position in each ear-lobe. That such cases of inheritance of a mutilation are admittedly rare does not necessarily prove that they are non-existent. The fact that (Windle, 1891) a fissure sometimes occurs in the sulcus intertragicus of the ear, as an arrest of development, scarcely seems an adequate explanation of the

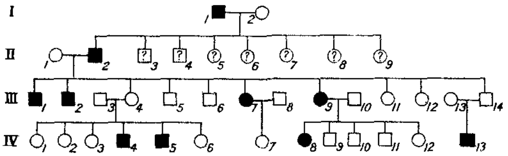


Fig. 67.—Pedigree Chart showing Inheritance of a Small Pit in the Left Ear.

above case; but in an instance cited by Windle, where the mother tore the lobule of her left ear when eight years old, and afterwards had eight children, one of whom, a boy, had cleft lobule of the left ear, there is obviously no inheritance involved.

Teeth.

Many abnormalities of the teeth are inherited, including some which are quite fixed from generation to generation, and others which are more variable. A short account is published (Thadani, 1921) of a Hindoo Amil community in India, in which a toothless type of man occurs. The men are not only toothless, but bald-headed and extremely sensitive to heat. The evidence, so far as it goes, indicates that the character is male-sex-linked. Anodont females are not at present known, but if daughters of a toothless father are married to a normal man, their male children are toothless (Bhudas). Fürst (1925) describes another case of anodontia. Wheelon (1925) states that congenital absence of upper incisors is rather common. He collected 20 cases in three years, and gives pedigrees which

suggest that the character is dominant. He describes three cases. In I., defects of the upper lateral incisors are transmitted through the female line. In II., the right upper lateral incisor is congenitally absent, and the same condition occurred in the mother and *her* mother, also in three sisters (on the left in one), two brothers, and a nephew. In III., the upper lateral incisors were lacking, and the same condition was found in the mother, *her* mother, four maternal aunts, one maternal uncle, one sister, and her daughter—*i.e.*, in four generations. In two individuals only one incisor was missing. The absences were accompanied with general nervous and other disorders which were independent of the dental defects.

It has often been assumed that dental caries is a result of civilised diet and the eating of sweets, but Schultz found it common in wild monkeys. The Eskimos, on the other hand, have magnificent perfect dental arches, such as are seldom seen in civilised peoples.

Ovazza* describes in two families the absence of all incisors. This condition was constant and behaved as a Mendelian dominant. Beadle (1926) gives a pedigree in three generations showing absence of certain teeth. They were also irregular in their time of eruption both of the deciduous and the permanent teeth, and in the number of teeth missing. The lacking teeth included both incisors and molars, but not canines. The condition occurred in both sexes and appears to be a simple dominant, five normal and five abnormal occurring in a family of ten. Those with tooth deficiency were dark-haired in 15 cases and light-haired in 3. This certainly suggests linkage with crossing-over between the genes for tooth anomaly and dark hair, and is worthy of further investigation.

A striking case of abnormal early decay and loss of teeth in three generations of a family is given by Sedgwick (1863). It is confined to the females (Fig. 68), and is inherited from mother to daughter. There is no evidence of it being transmitted by males.

Crosman (1927) cites from Guilford in 1883 a case of an edentulous woman without teeth or hair. She had a son in the same condition. He married a normal, and of their children six were normal and two had several undeveloped teeth. A normal sister had eighteen children, one of whom was without teeth or hair. McQuillan (1870) described a case

* *La Stomatol.*, 1922, xx. 21-23.

in which father, son, and grandson lacked the lateral incisor of the upper jaw. A second son had very dwarfed incisors, and part of his children were the same.

No doubt many other dental irregularities are inherited. But malocclusion and irregular teeth may result from crossing, unsuitable food, or malnutrition. Sinha (1918) gives a pedigree with 9 cases in three generations from a Hindoo family in Bengal. A man with *brown* teeth had three sons and three daughters with the same tooth colour, one son and one daughter being normal. One of the sons and one of the daughters transmitted this condition to the next generation. Hence it is a simple dominant.

Downs (1927) reports upon 647 clinical cases of dental defects from the Indiana Hospital for the Insane and the Indiana School for the Feeble-minded. They included cretins, Mongolians, dwarfs, giants, acromegalics, polyglandular

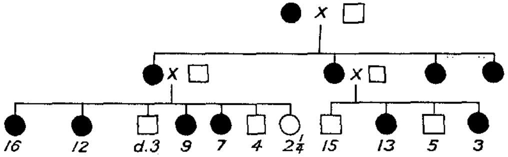


FIG. 68.—FAMILY SHOWING EARLY DECAY OF TEETH. THE NUMBERS BENEATH ARE THE RESPECTIVE AGES OF THE CHILDREN.

dyscrasias, hermaphrodites, microcephalics, goitrous, myxœdemas, etc., as well as normals. The dental anomalies found included missing laterals or other teeth, peg-shaped laterals, supernumeraries, spaced uppers, bunched lowers, prognathism, and normals. No definite relation was found between the presence of endocrine dyscrasia and dental anomaly, but dental anomalies were recurrent in several families and probably due to hereditary factors.

In a line of white rats whose ancestors had been treated for modification of the germ cells (Jones, 1924), two young with abnormal eyes were produced, and the condition was irregularly inherited. In the same line in a later generation a tooth anomaly appeared. The incisors grew into tusks which curved back into the mouth or over the lips. This was also inherited, while 500 controls showed neither condition.

Tails.

There is a considerable though scattered literature on tailless cats and dogs, which we will not attempt to summarise here. Bamber (1927) has recently reviewed the subject for cats, and Klodnitzky and Spett (1925) considered the matter in dogs. That congenital taillessness occurs in rats is less well known. Miss Conrow (1915) found three tailless rats which lacked all caudal vertebræ. One also lacked one or two lumbar vertebræ and all four sacral vertebræ. In all, the vertebral column ended far anterior to the posterior end of the body. The condition was congenital and not due to accident. Later (1917), by examining 71,500 rats at the Wistar Institute, where they have long been carefully bred for scientific purposes, she found nine tailless, and afterwards two more which were mated together.

The presence of a tail in man is an anomaly less rare than might be supposed. Bartels (1884) wrote an extensive monograph full of interesting lore on the subject of human tails. He pointed out that Pliny and Pausanius refer to tailed human beings. The existence of human races with a tail was formerly widely believed in, and the traditional devil may be regarded as a survival from these legends. The human embryo has a caudal appendage which, at one stage of its development, is one-sixth its total length; and if failure of absorption takes place the infant may be born with it attached. In Bartel's time over 60 cases, including some abnormalities of other kinds, had been recorded. Schaeffer (1892) added 25 more cases, but these were a very heterogeneous collection of anomalies. In the collected works of Robert Koch, vol. ii., p. 822, are two photographs of human beings with tails as long as a human foot. These photographs were taken by Koch in India in 1871, one a lad of seventeen, the other a child, but apparently they contained no bones. Schultz published in *Journ. Wash. Acad. Sci.*, 1925, a photograph of a twelve-year-old boy from French Indo-China with a tail nine inches long. A specimen also exists in the Royal College of Surgeons.

Ross Harrison (1901) reviewed the subject and described a case in detail. Some of these tails actually contain vertebræ, as well as muscles to move them. A baby girl was recently reported from Tennessee with a tail seven inches long, which appears to be a case of poetic justice. It has been pointed out that in the orang-utan the loss of a tail has pro-

ceeded farther than in man, since he only has two or three rudimentary coccygeal vertebræ while man has four or five or sometimes six.

A condition which corresponds to taillessness in mammals is rumplessness in fowls, in which the oil gland is absent and the caudal vertebræ are absent or only a remnant. Dunn and Landauer (1924) find that this condition may be due to (1) an accident in embryogeny, in which case it is not inherited, or (2) to a dominant factor. The two are phenotypically indistinguishable. Heterozygous rumpless fowls × normal gave 31 rumpless : 20 normal. In a later paper (1926) they find that the condition of homozygous rumplessness is viable, one such hen producing 17 similar chicks when bred to normal. Heterozygous rumpless × normal gave 245 rumpless : 267 normal chicks. Hence the condition is a simple dominant. It was also found that rumplessness segregated independently of dominant white feathers in 231 progeny from various matings.

LITERATURE

Bamber, R. C. 1927. Genetics of domestic cats. *Bibliographia Genetica,* iii. 1-86.

Bartels, M. 1884. Die geschwänzten Menschen. *Arch. f. Anthrop.*, xv. 45-131, pls. 2.

Beadle, O. 1926. An inherited anomaly of dentition. *Journ. Genetics*, xvii. 199-296, pl. 1.

Carrière, Reinhard. 1922. Über erbliche Ohrformen, insbesondere das angewachsene Ohrläppchen. *Zeits. f. Abst. u. Vererb.*

Conrow, Sara B. 1915. Taillessness in the rat. *Anat. Rec.*, ix. 777-783, figs. 3.

Conrow, Sara B. 1917. Further observations on taillessness in the rat. *Anat. Rec.*, xii. 155-159, figs. 3.

Crosman, A. M. 1927. Inheritance of abnormalities in teeth. *Journ. Hered.*, xviii. 368-370.

Dahlberg, G. 1923. Twins and heredity. *Hereditas*, iv. 27-32.

Dahlberg, G. 1926. Twin births and twins from a hereditary point of view. Stockholm: Bokförlags. *A. B. Tidens Tryckeri*, pp. 296, many figs.

Downs, W. G., Jr. 1927. Studies in the causes of dental anomalies. *Genetics*, xii. 570-580, figs. 3.

Dunn, L. C., and Landauer, W. 1924. Genetic and morphological comparison of two kinds of rumplessness in the fowl. *Anat. Rec.*, xxix. 143.

Dunn, L. C., and Landauer, W. 1926.

Fürst, Th. 1925. Der Erbgang bei Anodontie. *Arch. f. Rass.-u. Gessells.-Biol.*, xvi. 310-311.

Harrison, Ross G. 1901. On the occurrence of tails in man, with a description of the case reported by Dr. Watson. *Johns Hopkins Bull.*, xii. 96-101, figs. 6.

HILDÉN, K. 1922. Über die Form des Ohrläppchens beim Menschen und ihre Abhängigkeit von Erbanlagen. *Hereditas*, iii. 351-357, figs. 3.
HILDÉN, K. 1929. Studien über das Vorkommen der Darwinschen Ohrspitze in der Bevölkerung Finnlands. *Fennia*, lii., No. 4, pp. 39.
HOPF, LUDWIG. 1909. The human species. London: Longmans, Green.
JENKS, A. E. 1916. Pitted ear-lobes of congenital origin. *Journ. Hered.*, vii. 553-554, fig. 1.
JONES, ELIZABETH. 1924. The occurrence of an eye and of a tooth abnormality in a line of albino rats. *Anat. Rec.*, xxix. 142.
KINDRED, J. E. 1922. Inheritance of a pit in the skin of the left ear. *Journ. Hered.*, xii. 336-337, fig. 1.
KLODNITSKY, I., and SPETT, G. 1925. Kurzschwänzige und schwanzlose Varianten bei Hunden. *Zeits. f. ind. Abst. u. Vererb.*, xxxviii. 72-74.
LUSH, J. L. "Double ears" in Brahma cattle: another case of apparently simple Mendelian inheritance in farm animals. *Journ. Hered.*, xv. 93-96, figs. 2.
LYNCH, C. 1921. Short-ears, an autosomal mutation in the house mouse. *Amer. Nat.*, lv. 421-426.
McQUILLAN, J. H. 1870. Hereditary transmission of dental irregularities. *Dental Cosmos*, xii.
RITZMAN, E. G. 1921. Breeding earless sheep. *Journ. Hered.*, xi. 238-240, figs. 4.
SCHAEFFER, O. 1892. Beitrag zur Aetiologie der Schwanzbildungen beim Menschen. *Arch. f. Anthrop.*, xx. 189-224, pls. 2.
SCHOFIELD, R. 1917. Inheritance of a bilobed ear. *Journ. Hered.*, viii. 517-518, figs. 2.
SEDGWICK, W. 1861. On sexual limitation in hereditary disease. *Brit. and Foreign Med.-Chirurg. Review*, xxvii. 477-489, xxviii. 198-214.
SEDGWICK, W. 1863. On the influence of sex in hereditary disease. *Brit. and Foreign Med.-Chirurg. Review*, xxxi. 445-478, xxxii. 159-197.
SINHA, S. 1918. Tooth colour. *Journ. Hered.*, ix. 96.
THADANI, K. T. 1921. A toothless type of man. *Journ. Hered.*, xii. 87-88.
WHEELON, H. 1925. Clinical significance of the congenital absence of the upper lateral incisor teeth. *Endocrinology*, ix. 35-60, figs. 6.
WINDLE, B. C. A. 1891. Teratological evidence as to the heredity of acquired conditions. *Journ. Linn. Soc. Zool.*, xxiii. 448-502.
WRIEDT, CHR. 1919. Über die Vererbung von Ohrenlänge beim Schafe. *Zeits. f. Abst. u. Vererb.* xx. 262-263.
WRIEDT, CHR. 1921. Breeding earless sheep. *Journ. Hered.*, xii. 56.
WRIEDT, CHR. 1925. Die Erblichkeitsverhältnisse der ohrlosen und kurzohrigen Schafe und die Verbreitung dieser Typen in Norwegen. *Zeits. f. ind. Abst. u.-Vererb.*, xxxvi. 430-437, figs. 4.
YAMANE, J. 1915. On the inheritance of an aural abnormality in the Ayrshire cattle. *Journ. Coll. Agric. Tohoku Imp. Univ.*, vi. 166-170.

CHAPTER XIV

VARIOUS ABNORMALITIES AND DISEASES

HERE are included a variety of abnormal conditions not classifiable elsewhere. HARELIP and CLEFT PALATE are frequently found together. They have an extensive medical literature, but our knowledge of their inheritance is not satisfactory as the pedigrees are usually rather fragmentary. Rischbieth (1910), in a study of these malformations, collated the data regarding their incidence. Frobelius examined 180,000 children in the Foundling Hospital of St. Petersburg during thirty years, and found one or both conditions in a total of 118 cases, or 0·066 per cent. Among 67,945 children examined at a London Hospital in 1908, thirty-nine showed the deformity in one form or another, hence a frequency of 0·057 per cent. But this figure is too high, because some children attended more than once. The condition is often associated with other deformities.

Mason (1926) gives a recent pedigree showing irregular inheritance in four generations, skipping a generation in one case. Other pedigrees may suggest a recessive or a dominant character but with irregularities. Birkenfeld (1926) discusses the subject medically and statistically. His pedigrees show that these defects are more often passed from father to son and from mother to daughter than from one sex to the other. He investigated 204 cases, but was unable to get evidence of heredity in more than 20 per cent. In 34 cases the inheritance was recessive and in 8 dominant, and in one instance transmission was from mother to son, as well as daughter. Manson (1928) describes a family in which two cases of hare-lip and cleft palate appeared in two members of a family of fourteen whose parents were normal. In another family with normal parents these defects appeared in five members (both sexes) of a family of ten. These cases suggest at any rate a recessive condition.

Benjamin and Stibbe (1926) describe a threefold disturbance in the development of the nose—(1) dilation, (2) bifid form, (3) absence of proper bone. The pedigree shows six families in two generations containing 14 affected : 14 normal sibs. The

condition of the previous generation is unknown, but this abnormality appears to be a simple Mendelian dominant.

F. Weiss (1929) briefly records a family in which the males have adherent tongues. The tongue could be protruded but not elevated, resulting in defective speech. In a family of 4 sons and 4 daughters, the latter all had normal speech, while the sons all showed the defect. The father of this family had the defect. He also belonged to a family of 4 boys and 4 girls, the former defective, the latter normal. His uncle also had defective speech. If this record is correct, there were nine cases in three generations, all the males being defective and the females normal in two successive generations. This would indicate male-to-male inheritance through the Y-chromosome, but the case obviously requires further investigation.

Lundborg (1920) concludes that hereditary DEAFMUTISM is due to one Mendelian recessive factor and rejects Plate's hypothesis of two factors. Acquired deaf-mutism may be either intra- or extra-uterine in origin. Hence congenital deafness is not always hereditary. Irish statistics of the year 1891 register congenital deaf-mutism as 76 per cent. of all cases. In Norway (1897) the number was estimated at 50·9 per cent., in Sweden (1904) at 40·8 per cent., and in the Malmöhus district of Sweden (1919) at only 28·2 per cent. (108 in 383). Government statistics of deaf-mutes (Washington, 1920) show that they are more frequent in negroes than in any other race in the United States.

Meningitis and scarlatina are said to be the most common causes of acquired deaf-mutism. In addition to the difficulty in distinguishing between genotypical (inherited) and phenotypical (acquired) deaf-mutism a statistical error is introduced by the fact that in small families the children may all be normals, even when the parents are heterozygous for the condition. Since these children are not added to the offspring of matings of heterozygotes, the result is more than 25 per cent. of abnormals. This can be corrected by applying the formula of Weinberg, and it then closely approximates to the expected 25 per cent.

From Fay's evidence of marriages of the deaf in America (1898), twenty-two families had four to nine children each, all deaf. The children numbered 112. Hence it appears that genotypical deaf-mutes will have only deaf-mute children, and from this and other evidence it appears that the character is probably a simple recessive. The difficulty in all statistics

on this subject is to distinguish between genotypic and phenotypic deaf-mutism. Love (1920) also reaches the conclusion that sporadic congenital deafness is inherited as a Mendelian recessive, from a study of an Ayrshire family which has branches in America and Australia. This family shows five affected generations descended from a common ancestor three generations further back. Yearsley (1920) gives an account of a family with a history of "acquired" deafness, which produced offspring born deaf. But as the acquired deafness is apparently hereditary otosclerosis, this is merely a case of the earlier appearance of the abnormality. Horne (1909), in a study of deaf-mutism, says that the number of deaf-mutes in Europe is estimated at about 1 in 1,350 of the population. In England the frequency (from statistics) is 1 in 2,043, Scotland 1 in 1,860, Ireland 1 in 1,398. Seven pedigrees are recorded, but there is no separation of heredity and acquired cases.

Kraatz (1925), from a study of several pedigrees of hereditary deafness due to deaf-mutism and otosclerosis (a frequent cause of deafness in later life) and from the data in Fay's *Marriages of the Deaf in America*, where the records of 4,471 marriages of the deaf are given, concludes that deaf-mutism cannot be due to a single dominant, recessive, or sex-linked factor, but that all the statistics except a few irregular ratios fit the theory of two recessive factors. As expected on this basis, deaf × deaf may give all normal children in some families. Manson (1928) gives two short pedigrees with 5 and 3 cases respectively in three generations, and the results so far as they go are in accord with this tentative hypothesis.

Albrecht (1925) points out the impossibility of determining the method of inheritance from purely statistical data, and classifies deaf-mutism into six types due to different causes, some types of the defect being inherited and some not. No doubt when the various types of acquired and congenital, inherited and non-inherited deaf-mutism are more fully analysed and their inheritance traced, the laws of inheritance will be recognised. But as yet there has been insufficient recognition of the many diverse causes that lead to congenital deaf-mutism as well as the acquired types of deafness.

There are various early records of the inheritance of POLYMASTIA, or multiple breasts. This term is confined by some to extra breasts on the chest, others include swellings in the axillæ which enlarge during lactation. Windle (1891) describes several cases in mother and child.

Klinkerfuss (1924) gives a pedigree of a family with 5 cases in four generations, inherited from mother to daughter and not present in the men. One of the women had a swelling in the left axilla during pregnancy, without nipple or areola. Another had a swelling in each axilla, the left being 5.5 cm. in diameter with a perfect nipple and secreting milk during lactation. That in the right axilla measured 9 cm. in length. In the last generation, a child of two has a nodule in the left axilla 1 cm. in diameter, with nipple and areola. That similar variations occur in man is shown, for instance, by a case (Evelt, 1892) of a man with two smaller nipples symmetrically placed below the normal ones. Castle (1924) gives an account of Graham Bell's success in producing a flock of multinippled sheep by selection and breeding for extra nipples, sheep with as many as six being produced.

Elephantiasis may be congenital or it may appear later in life. In inheritance it appears as an irregular dominant. Lyon (1925) describes a case in which the ancestors were dropsical as far back as the great-grandmother. The mother suffered from dropsical swellings of the feet during pregnancy. The child was prematurely born and its legs and feet were much swollen at three months. At two years of age it got better, but at thirteen was very subject to swollen legs with a watery exudation when wounded. The inherited tendency is toward lymph stasis.

That inheritance may lead to the complete absence of an essential organ of the body is shown by the work of Bagg (1924) on mice. In the descendants of mice which had been subjected to light doses of X-rays, among 300 autopsied animals were 50 having a single kidney. Hereditary abnormalities also appeared in the eyes, feet, and other parts. Matings between animals with one kidney gave small litters in which several young died in the first week. The offspring of a mating between a male mouse with one kidney and blind in the right eye, and a female normal but heterozygous for such defects are fully described. Two died within twenty-four hours. They lacked both kidneys. One had a defective left eye. The remaining five were active, and apparently in good nutrition. Three of them were killed and examined twenty-four hours after birth. A female with defective left eye had no kidneys, one male had only a very small remnant of renal tissue on one side, another had normal kidneys. The two other males were kept on and proved to be normal. Hence, of this litter three

had normal kidneys, three had no kidneys, and one a remnant.

Pyloric stenosis, or constriction of the pyloric end of the stomach, is recorded once as occurring in successive generations, although it has very frequently been observed in two or even three sibs. It is accompanied by violent vomiting in infancy. Caulfield (1926) cites a case in which father and infant son and daughter all had it. Buttersack (1927) describes the inheritance of Hirschsprung's disease (congenital hypertrophy and dilation of the lower part of the colon). The grandparents suffered severely from gastro-intestinal trouble. Three of their children were sound and a son had Hirschsprung's disease. He transmitted it to a son, but his normal brother and sister each had a child (the former female) afflicted.

Hereditary disorders of bone development have been studied in a monograph by Stocks and Barrington (1925). Abnormal outgrowths of exostoses of bone are known even in Neolithic skeletons, and have been recorded in the horse, cat, dog, lion, and in fishes. In man their inheritance has only been recorded in the last fifty years. About 64 per cent. of the known cases of multiple exostoses have at least one relative affected. Inheritance is usually from the affected parent, this being the father in 73 per cent. of such cases. Transmission by an unaffected male is unproven, but in about one-quarter of the cases of female transmission she is unaffected.

Enchondromata may be inherited either associated with or without exostoses. Most of the pedigrees they have collected show the condition in every generation, inherited as a dominant, but occasionally it appears suddenly without any evidence of its existence in the previous ancestry, and it is much more frequent in males than females.

A condition of partial failure of ossification of the membrane bones, which is complementary to the above in some sense, is known as cleido-cranial dysostis. Its effects are chiefly seen in the head and clavicles. The failure of the clavicles to ossify gives an extraordinary mobility to the shoulders, so that they can be placed almost in contact. It is a rare condition and the earliest case on record is in 1765. In all, 144 cases have been recorded. The cranial vault and facial bones are also often deformed, but the head bones may be normal. Ninety-six of the cases are seen to be hereditary, 62 ♂, 33 ♀, 1, sex not stated. The sex-ratio of 65 per cent. is very similar to that for exostoses. In 48 cases, belonging *equally* to both sexes, there is

no evidence of inheritance, and some appear to arise *de novo*. It appears usually as a dominant in inheritance. As with exostoses, when the father transmits, the sex ratio of the children is high (68·6 per cent.), when the mother transmits, 48 per cent., suggesting some form of sex-linkage.

Brittleness of bones has been considered elsewhere in connection with blue sclerotics (*q.v.*), but it may also occur independently of that ocular defect. Known as OSTEOPSATHYROSIS, it is a remarkable congenital weakness which appears to be inherited as a dominant character. In one recorded case (Conard and Davenport, 1915) a boy suffered at least twelve fractures of his limbs before reaching the age of three years, being born with both thighs broken. Later this extreme liability to fracture began to diminish, but that it may still remain a serious defect in the adult is shown by the fact that the mere tension of the muscles or weight of the body, as in dancing, may be sufficient to cause a fracture. Twins may be born in families having the peculiarity, one showing the defect and the other normal. Sedgwick (1863) cites a family from Dr. Pauli with a less extreme form of the condition, in which the brittleness was confined to the bones of the upper extremities. It occurred in three generations.

CONGENITAL DISLOCATION OF THE RADIUS is described in four generations in two families and three generations in another. Isolated cases of this defect are not uncommon, but it is rarely inherited unless associated with other defects. A rare form of osseous dystrophy is cited, causing deformities of the limbs in a father and two children. Hereditary osteitis of the lower limbs is another rare condition cited, eleven males with the defect occurring in four generations of one family.

An American family is described by Goldsmith (1922) in which there are two round openings in the parietal bones at the back of the skull. These sometimes form a single opening in the younger stages, and in some cases it may later close up entirely. It is clearly a failure to complete development. In five generations of this family 16 cases are known. The manner of its inheritance is not clear. Microcephalic people occasionally occur in families (Bernstein, 1922). There is often more than one such child in a family, but they seldom occur in successive generations, and nothing appears to be known concerning the inheritance of this condition.

Muscular Defects.

While numerous muscular variations have been recorded in man, little is known of their inheritance. The STERNALIS muscle is present in about 4 per cent. of individuals. Dmitrevski-Zassedateleva (1927) found it in two cadavers among 350, bilateral in one. It is one of the so-called cutaneous muscles and was connected with the sterno-cleido-mastoideus by tendinous fibres and with the pectoralis major by a distinct muscular fascicle.

Suppression of the PALMARIS LONGUS muscle of the forearm is apparently inherited as a dominant, according to Thompson, McBatts and Danforth (1921). Its presence or absence can be observed in the living subject, and its inheritance was studied in 102 white families and some Indians. Several pedigrees show its absence from one or both arms in two or three generations. Of 365 white men, 43 lacked the muscle in both arms, 17 in the left, and 19 in the right. Of 401 white women, 75 lacked it in both arms, 21 in the left, and 25 in the right. The percentage of absence from one or both arms was 19·5 per cent. for ♂♂, 29·1 per cent. for ♀♀; from negroes, 2·5 per cent. for ♂♂, 7·6 per cent. for ♀♀; for Japanese sailors 12 per cent.

There are a number of pedigrees of PERONEAL ATROPHY, which is due primarily to a nervous defect. Herringham (1889) described a family in which not only the legs were affected, but also generally the forearm and hand. It was probably transmitted as a sex-linked recessive, except in one case where an affected father transmitted it to a son. This may have been distal myopathy, and the method of inheritance is different from that of later pedigrees. Macklin and Bowman (1926) fully describe a modern case, with a pedigree of 101 descendants of an orphan who emigrated to Canada when young. In five generations 21 affected individuals appeared. The atrophy is confined to the peroneal and calf muscles. There is a definite line above the knees, between the cold cyanotic and roughened skin over the wasted muscles and the normal skin above. The disease makes its appearance between the ages of twelve and forty years, and individuals may transmit it before the symptoms appear in themselves. Of 25 persons who reached the age of forty and had an affected parent, 11 were affected and 12 normal. The condition is clearly a simple Mendelian dominant. Mating

between two affected persons has never taken place, and the gene would probably be lethal in the homozygous condition. The pedigree shows anticipation, or a tendency to develop at an earlier age in later generations. Parker (1928) gives another pedigree in four generations, with 54 descendants of a great-grandfather, 21 of whom were affected while some others are not yet old enough to show the defect. A simple dominant is indicated here also. The syndrome was first recognised in 1886. Wasting usually begins in the second or third decade of life, in the feet or peronei, gradually extending up the limbs. Occasionally it appears first in the hands. The trunk is not affected.

Lundborg (1913) described MYOCLONUS-EPILEPSY in an extensive monograph of a peasant family in south-eastern Sweden, including 2,232 individuals in seven generations between the years 1721 and 1907. The disease appears during life and leads to death in middle age. It begins as epilepsy, with later myoclonic phenomena (spasms of contraction in various muscles), and in one line PARALYSIS AGITANS. The material included 377 families (sibships) and 1,909 births. There was much intermarriage, 35 per cent. of the parents being related. A full description is given of the other pathological conditions, including nervous and mental diseases, epilepsy, weak mentality, idiocy, and debility. There were 17 cases of myoclony in nine families. The inheritance is clearly a Mendelian recessive. For the paralysis agitans no method of descent could be determined. The 2,232 individuals examined are grouped as follows: (1) Eleven families DD × RR, with 166 children, all normal; (2) eleven families DR × DR, with 93 children, of whom 77 reached an age of over fifteen years. Of these, 24 or 31·2 per cent. were abnormal. Applying the statistical correction of Weinberg gives 21·8 per cent. abnormal (expectation 25 per cent.); (3) DR × RR, 5 families with 46 children, of which 40 reached over fifteen years of age. Twenty of these were normal, or 45·3 per cent. with the statistical correction. This is the only Swedish family known to have the peculiarity, and the results are in very good agreement with Mendelian expectation.

Lundborg concludes that the tendency to degenerative diseases is due to bad racial quality in this part of Sweden, to much inbreeding (which, of course, brings out the recessive conditions) and to the strong use of alcohol. The high birth-rate and the excess of coffee drunk were also regarded as

unfavourable forces. But inbreeding by itself is sufficient to bring out any deleterious recessive factors present.

MYOTONIC DYSTROPHY, or wasting of muscles owing to nervous defect, is essentially the same condition, which has been fully investigated within the last fifteen years. It is a characteristic family-degenerative disease belonging to the same group as ataxia, spastic paraplegia, certain forms of muscle atrophy, progressive bulbar paralysis, amaurotic idiocy, Thomsen's myotony, hereditary optic atrophy, etc. Myotonic dystrophy is distinguished from Thomsen's myotony by the presence, besides myotonic symptoms in certain muscles of the hand and tongue, of atrophy of muscles especially of the lower arm, face, neck, and of the peroneal muscles. In addition there are other dystrophic symptoms, such as emaciation, presenile cataract, baldness, disturbances in bone development, atrophy of the testes or the thyroid, with psychological and moral derangements which are believed to point to disease of the endocrine glands. The frequency of cataract leads the patient to the ophthalmologist. The disease can be inherited through apparently sound generations and finally appear simultaneously in the different branches of a family, as though a progressive development of it had been taking place. Fleischer (1922) has studied peasant families in Würtemberg through the church registers, and constructed a pedigree of 1,429 persons in 233 families, all descended in six or seven generations from a single couple in the eighteenth century. They were probably unrelated and had eight children of whom six had children giving rise to as many different lines of descent (A B C E F H). In the A line there were no degenerative symptoms found except one woman with cataract, three epileptics from related parents and one goitrous imbecile. In the B line certain degenerative characters appeared, childlessness in two, and in another high infant mortality and children lacking in mental development. In the C line no degeneration appeared except infant mortality and early death of mother and son. In E, which is most numerous, all eight branches show degenerative symptoms. Some branches develop myotonic dystrophy, high infant mortality, childlessness, and an accumulation of degenerative nervous conditions including weak intelligence. In the F line of descent certain children develop severe myotonic dystrophy, many are sound but some lines show early death or few children. In the H line are few if any abnormal symptoms. Thus in this plexus of families descended from an original pair, degenerative

phenomena appear in two of the eight lines of descent, and especially in the fifth, sixth, and seventh generations of the lines showing myotonic dystrophy.

Frey (1925) has made a study of a similar pedigree on a smaller scale in Switzerland, where the condition is not uncommon, being known in ten cantons. Myotonic dystrophy is found in all countries and about 200 cases have been described. It appears to be inherited in a latent condition through four generations, then suddenly appears and remains dominant for several generations. In the present pedigree there were 35 cases; 17 were personally investigated, and of these 12 had myotonic dystrophy, 5 simply dystrophy. The transmission was traced through over eight generations.

Minkowski and Sidler (1928) have studied 13 cases of muscle dystrophy, and find much variation in the symptoms. In every case, the ancestors were found to be related when traced back through a number of generations. In these pedigrees the parents and ancestors are always normal, the inheritance recessive, one or two sporadic cases appearing at the end of each pedigree.

A condition which is said to be rare is HEREDITARY TREMOR. Bergman (1920) states that 50 families showing this condition are mentioned in the literature. It consists in rapid involuntary and rhythmic contractions of certain groups of muscles. Usually the arms and hands are affected, but sometimes also the head or legs or the whole body. Hereditary tremor most frequently appears in early youth, and often increases in intensity later. It generally ceases during sleep and perfect rest. Sometimes it appears only at times of exertion or emotion. The tremor may be rapid (8 to 10 vibrations per second), or slower (3 to 4 per second). People with hereditary tremor are often nervous and emotionally unstable. The handwriting is affected, and may be almost or quite illegible. Bergman traces this condition through three generations (four individuals) in a Swedish peasant family. The condition is probably similar to paralysis agitans, which is said to be due to the degeneration of the parathyroid gland.

ATAXIA in pigeons is apparently a very similar condition. In 1914 Riddle (1918) obtained in breeding experiments a female pigeon with marked lack of control over the voluntary movements of head and body. It appeared, probably as a mutation, under conditions of "reproductive overwork," in which the bird is obliged to continue laying by removing the

eggs; and the condition has been inherited through five generations. About 175 young have been reared, and of this number 119 were classified as normal and 46 as affected. From these and other matings the evidence indicates that ataxia is inherited as a simple recessive with some irregularities. Affected birds show quivering movements, nodding heads, unsteady gait, and irregular flight in various degrees. Koch and Riddle (1918) analysed the brains of ataxic birds in comparison with the normal. They found in the former higher values for water content, protein, and extractive sulphur, with lower values for lipoids, phosphatids, and cholesterol. The results suggest a chemical immaturity or under-development of the affected brain, more like those of normals at a younger stage of development, but further investigations of this subject are desirable.

Drinkwater (1914) described an interesting case of BIMANUAL SYNERGIA, in which the individual is obliged to move both hands and arms in the same direction at the same time. Only four other cases of this rare condition are known in the medical literature, and they were all recorded in Germany. In Drinkwater's case, if the boy held a pencil in each hand and wrote with the right hand, the left would produce the same words in mirror image form. Attempts to move one hand when the other was held caused acute pain. This case was unique in that the synergia was accompanied by similar sensations in both hands when only one was stimulated, the unstimulated member feeling the sensation more intensely. Crossing of sensations also occurred. Thus, when a hot-test tube was held in the right hand, and a cold one in the left, the left hand felt hot and the right cold.

The motor phenomena in this case were traced through 9 individuals occurring in four generations. The manner of inheritance is that of a Mendelian dominant, except that one woman, four of whose ten children showed the condition, did not exhibit it herself. She probably, however, was affected in infancy and outgrew it. Every infant has to learn to use its right and left limbs independently, and this power of unilateral control develops earlier in some individuals than in others. One boy in this pedigree was able to overcome the synergia at the age of fifteen years, after repeated efforts. The condition is, then, essentially one of failure in development of a particular function.

CANCER.

Our present knowledge of cancer is much too uncertain to permit of a general discussion of the inheritance of cancer in man. But there is a considerable amount of experimental work with animals which has given definite results, and there are some definite facts regarding the occurrence of cancer in man to which reference may be made. Some of the earlier work is referred to by L. Loeb (1921). The inheritance of specific kinds of cancer in rats and mice and other animals is known—*e.g.*, cancer of the inner canthus* of the eye in cattle, cancer of the scrotum in rats, and sarcoma of the thyroid in rats. Miss Slye has shown the inheritance of cancer of the liver and other special forms of cancer in certain families of mice. I am informed that the late Professor Plummer recorded cancer in three generations of wolves in the Zoological Gardens, occurring always in the same place—viz., the shoulder. Loeb concludes that the endemic occurrence of cancer in animals is due to hereditary transmission of the disposition to cancer. Infection from parasites may, in addition, act as an external stimulus, comparable with X rays.

In Drosophila a series of tumours inherited in certain stocks have been described by I. T. Wilson (1924). Lethal 7 of Bridges was shown to be due to a tumour. Miss Stark found that the tumour develops from embryonic rudiments destined to form adult organs during the pupal stage and accompanied by melanin formation. Another tumour in the same stock is hereditary, but benign and non-lethal. Wilson describes other tumours in Drosophila, including two new types. They are all hereditary and all develop from larval tissue and deposit black pigment. These four types differ in time of location, number, cell structure, malignancy, and mode of inheritance. Two other types depend on recessive multiple factors for their development. One is partly dependent on environmental conditions, and a second is to a less degree.

It is well known that tumours or cancers can be induced in mice by the application of tar or certain other irritating substances to their skin. Some of these are skin tumours, but for some unknown reason the majority are in the lung. If the cancer produced in a tarred mouse is removed, it is very difficult or impossible to produce another in the same animal. This

* The angle next the nose where the eyelids meet.

indicates some form of acquired immunity. Hanau, as early as 1889, successfully transplanted carcinoma from one individual to another of the same species. Leo Loeb and Maud Slye have done much work on the subject in America. The interval between tarring and the production of a tumour in mice is about one-third the life span, or equivalent to fifteen or twenty years in man. In mice, and in man as well, there is a cancerous diathesis affecting the body as a whole, and also a heritable liability for some particular organ to be attacked. Slye (1926) found that in crossiug a normal female with a male having lung carcinoma the F_1 was normal. The F_2 showed four homozygous non-cancerous : six heterozygous non-cancerous : three with cancer. In 300 such crosses susceptibility to cancer behaved always as a simple Mendelian recessive. She took seventeen years to get a cancer-bearing stock, and her conclusions are based on over 5,000 neoplasms, including nearly every type known to human pathology. The breeding experiments involved nearly 65,000 mice, and in every case the inheritance was recessive. These results are unique at present and are much in need of confirmation. But there is nothing improbable in the presence of sharp differences of susceptibility to tumour formation in different individuals of the same species. In plants, such inherited differences in susceptibility are known in the relation of wheat rust to wheat, and in the resistance of sunflowers to the attack of Orobanche, and of some potato varieties to wart disease.

Miss Lynch (1928) has also studied the inheritance of susceptibility to tar-induced tumours in the lungs of mice. She found a strain of mice in whicb the frequency of lung tumours was 6·7 per cent. (in 208 animals), and another in which it was 37 per cent. (in 135 mice). After painting the skin with tar the difference in frequency of tumours remained, though both were higher, 22 per cent. and 85 per cent. respectively. Possibly the latter were all susceptible if a better method of inducing tumours had been employed. These strains were crossed, and 28 F_1 mice gave 79 per cent. of lung tumours. The F_1 backcrossed to the two parental strains gave respectively 39 per cent. and 81 per cent. with tumours. The conclusion drawn is that susceptibility to tar-induced tumours is hereditary and that the number of factors involved in this case is unknown, but they may be multiple. Her work is not so long-sustained nor perhaps so consistent as that of Miss Slye, but evidently more work is needed before the inherit-

ance element in connection with tar-induced tumours can be regarded as settled.

Leo Loeb (1923) reported the results of an investigation of the inheritance of cancer in mice, involving a complete record of about 12,000 female mice. He concludes that the cancer rate of each strain is characteristic and transmitted by heredity to successive generations, usually with surprising regularity. The tumour rate in different strains varies from zero to nearly 100 per cent. The rate of tumour formation may also vary within a strain, owing to (*a*) decrease of fertility and vigour through long inbreeding, (*b*) unavoidable selection within the strain. In crosses between strains, the F_1 is variously intermediate in tumour-rate, but higher tumour-incidence was often dominant. The age at which tumours appear is also characteristic of different strains, and the differences are inherited. Generally in strains with a high tumour-rate the tumours also appear earlier in life, both conditions being due to an intensity factor. There is also in certain strains a tumour-rate which is independent of tumour-age.

While the cancer-rate in mice is not in general a sex-linked character, yet in certain cases a sex-linked factor may enter as one of the multiple factors which determine cancer inheritance. But no cancer can originate without the ovarian secretion, so that the activity of the ovary is an important controlling condition, and if the secretion is eliminated mammary cancer is practically prevented.

It may be assumed that in man the conditions are similar in principle to those in animals. Preiser and Davenport (1918), show that the tendency to multiple NEUROFIBROMATOSIS* (also known as von Recklinghausen's disease) behaves as a dominant in heredity, though it sometimes skips a generation. This condition is rare, being found in only one in 2,000 cases. Loeb concludes that in man probably one or more factors are hereditarily transmitted which determine the intensity of the tendency towards cancer development. In many cases cross-breeding appears to have equalised this tendency in man. But in Norway there is evidence of marked differences in the tendency to cancer in different strains and races.

In England, Holland, Switzerland, and Japan the death-rate from cancer is about the same, the total incidence being similar for the two sexes but differently made up. Thus in

* The formation of numerous tumours from nerves and containing connective tissue.

men there is a high rate of cancer in the alimentary canal, and in women cancer of the breast and uterus are common, although both rarely occur in the same individual. In Japan, cancer of the breast is unimportant, but cancer of the uterus is so much more common that the mortality from both is higher than in Holland or Switzerland. Little (1923) concludes on statistical grounds that the tendency to formation of cancer in man is inherited. In a general population there were 44,593 non-cancerous and 274 cancerous, or 0·61 per cent., while in the progeny of one cancerous parent there were 2,747 non-cancerous to 63 cancerous, or 2·24 per cent. But, of course, it might be argued that this was due to infection or to similar environment. Auvray (1927) cites several cases in which cancer of the same organ occurs in man for three or four generations. In one family it was of the intestine; in another, of the ovary; in another, of the uterus in the first, second, and third generations; and of the rectum in the fourth. In the pedigree it also occurred at progressively earlier ages.

Strong (1926) cites a cancer family from Wortlin, with a pedigree of cases in six generations. He concludes that the inheritance is recessive, but it could equally be explained as a dominant. Of course, it is possible that, as with other abnormalities, the manner of inheritance is not always the same. Pearl (1928) publishes a pedigree of human cancer in eight members of a family in three generations. This is 196 times the frequency in the population. He reports on 816 cases of malignant tumours among the autopsies in the history of Johns Hopkins Hospital. It is found to be two or three times more frequent in whites than in coloured people. It was long ago pointed out that there is an antagonism between tuberculosis and cancer. Those organs having tuberculosis in man are rarely sites for cancer, and rarely do cancer and tuberculosis occur together in the same individual. They also differ in that cancer generally has a higher rate in females and tuberculosis in males; cancer is generally later and tuberculosis earlier in life; cancer is usually of lower and tuberculosis of higher frequency in the coloured race.

Manson (1928) gives a striking pedigree of hereditary sarcoma. A mother died of lymph-sarcoma on the left side of the neck at the age of twenty-nine. Her husband was normal and there were three sons. One son (C.) died at the age of sixteen from sarcoma on the left side of the neck, and another (T.) died at nineteen after two operations for sarcoma in the

same position. The husband's mother had two sisters who died of cancer of the breast at an advanced age. This case suggests that two independently inherited factors may be involved. Clinically and microscopically the evidence is complete that the cases in the mother and her two sons were the same—*i.e.*, round-celled sarcoma of the lymph gland in practically the same position. C. was born after the mother showed signs of the disease. T. was less in touch with C. (who first showed it) than any other member of the household, and very much less than W., a brother who was closely in contact with C. but remained normal. There seems to be no escape from the direct inheritance in this case.

It is recognised that tumour growths are more common in unspecialised tissue, such as connective tissue and epithelial cells, while the highly specialised cells usually escape.

TUBERCULOSIS.

Reference may be made here to the studies of tuberculosis by Pearson (1907) and Goring (1909). They compared the correlation between parent and offspring as regards the incidence of the disease with that between husband and wife, in order to determine the relative importance of inheritance and infection in the development of the disease. Pearson found a correlation of 0·5 between parent and offspring, which is about the same as for such characters as eye colour, height, etc., indicating the same tendency to inheritance. Husband and wife, on the other hand, gave a correlation of 0·24 and much of this was believed to be due to assortative mating. Pearson's data were taken from the upper classes. Goring studied British convicts, and also found a correlation of 0·5 for parent and offspring, but none for husband and wife.

Govaerts (1925) studied the hereditary factor in the ætiology of tuberculosis. In 214 families a total of 5,629 individuals were observed, and it was concluded that hereditary resistance to tuberculosis played a determining rôle in the ætiology. Percy Stocks (1927) brings fresh evidence of the inheritance factor. From examination of 4,000 tuberculous persons in Belfast, he found that the fathers and mothers of tuberculous patients had a higher rate of tuberculosis than the general population. This excess was much more pronounced when both parents were tuberculous.

Wright and Lewis (1921) have made experiments on guinea-

pigs, in which they found marked differences in resistance to tuberculosis in a number of inbred families. The high resistance of one family was transmitted by either sex to the offspring in crosses with other inbred families. It is found that the factors determining resistance to tubercle are not closely related to the other elements of vigour, such as growth-ratio, adult weight, frequency and size of litter, percentage of young born alive, and percentage of young raised to weaning. Inbreeding brings out differences between families in these characters, as well as independently in resistance to tuberculosis.

It was formerly widely held (Sedgwick, 1863) that LEPROSY is hereditary, but that it descends by collateral lines and frequently skips a generation. There is quite possibly an inherited constitutional diathesis towards this disease as towards some others. The lepra bacillus is known, just as is the tubercle bacillus, but there may, equally with tuberculosis, be constitutional differences in the resistance to its attacks.

LITERATURE

ALBRECHT, W. 1925. Zur Vererbung der Konstitutionellsporadischen Taubstummheit. *Arch. f. Ohrenheilk.*, cxii. 286-291.

AUVRAY. 1927. A propos de l'hérédité du cancer. *Bull. de. l'acad méd. Paris*, xcvii. 420-423, 441-442.

BAGG, H. J. 1924. The absence of both kidneys associated with hereditary abnormalities in mice. *Proc. Soc. Exp. Biol. and Med.*, xxi. 228-229.

BENJAMINS, C. E., and STIBBE, F. H. 1926. Een merkwaardig Geval van aangeboren Afwijking van den uitwendigen Neus. *Nederl. Tijdschr. v. Geneesk.*, lxx. 2543-2549.

BERGMAN, EMANUEL. 1920. A family with hereditary (genotypical) tremor. *Hereditas*, i. 98-106.

BERNSTEIN, CHAS. 1922. Microcephalic people, sometimes called "Pin heads." *Journ. Hered.*, xiii. 30-39, figs. 4.

BIRKENFELD, W. 1926. Über die Erblichkeit der Lippenspalte und Gaumenspalte. *Arch. f. klin. Chir.*, cxli. 729-753.

BUTTERSACK, P. 1927. Über familiäres Vorkommen der Hirschsprungschen Krankheit. *Münch. med. Wchnschr.*, lxxiv. 1626-1628.

CASTLE, W. E. 1924. The genetics of multinippled sheep. *Journ. Hered.*, xv. 75-85, figs. 2.

CAULFIELD, E. J. 1926. Familial incidence of pyloric stenosis. *Amer. Journ. Dis. of Children*, xxxii. 706-708.

CONARD, H. S., and DAVENPORT, C. B. 1915. Hereditary fragility of bone (Fragilitas osseum, Osteopsathyrosis). *Eugenics Rec. Office Bull.*, No. 14, Cold Spring Harbour, pp. 31.

DMITREVSKI-ZASSEDATELEVA, E. N. 1927. A contribution to the origin of the musculus sternalis (m. præsternalis) in man. (Russian, English summary). *Journ. Russe d'anthrop.*, xvi. 34-39, fig. 1.

Drinkwater, H. 1914. Obligatory bi-manual synergia with allocheira in a boy otherwise normal. 17th Internat. Congress Med., London, (1913), 117-124.

Evelt, Ernst. 1892. Ein Fall von Polymastie beim Mann. *Arch. f. Anthrop.*, xx. 105-112, pl. 1.

Fay, Edward A. 1898. Marriages of the deaf in America. Volta Bureau, Washington, pp. 527.

Fleischer, B. 1922. Untersuchungen von sechs Generationen eines Geschlechtes auf das Vorkommen von myotonischer Dystrophie und anderer degenerativer Merkmale. *Arch. f. Rassen. u. Gesells.-Biol.*, xiv. 13-39, figs. 14.

Frey, Hans C. 1925. Beitrag zur myotonischen Dystrophie. *Arch. f. Rassen. u. Gesells.-Biol.*, xvii. 1-46, pl. 1 and pedigrees.

Goldsmith, W. M. "The Catlin Mark": The inheritance of an unusual opening in the parietal bones. *Journ. Hered.*, xiii. 69-71, figs. 5.

Goring, Chas. 1909. On the inheritance of the diathesis of phthisis and insanity. London: Dulau, pp. 28.

Govaerts, A. 1922. The hereditary factor in the etiology of tuberculosis. *Eugen. Rec. Office Bull.*, No. 23.

Govaerts, A. 1925. The influence of heredity in the etiology of tuberculosis. *Eug. Review*, xvii. 12-22.

Herringham, W. P. 1889. Muscular atrophy of the peroneal type affecting many members of the same family. *Brain*, xi. 230-236.

Horne, Jobson. 1909. Deaf-mutism. *Treas. Human Inheritance*, pp. 27-29, pl. 1, pp. 69-72, pls. 2, pp. 124-126, pl. 1.

Klinkerfuss, G. H. 1924. Four generations of polymastia. *Journ. Amer. Med. Assn.*, lxxxii. 1247-1248.

Koch, Mathilda L., and Riddle, Oscar. 1918. The chemical composition of the brain of normal and ataxic (?) pigeons. *Amer. Journ. Physiol.*, xlvii. 124-136.

Kraatz, J. J. 1925. Hereditary deaf-mutism. *Journ. Hered.*, xvi. 265-270, figs. 3.

Little, C. C. 1923. The inheritance of a predisposition to cancer in man. *Eugenics, Genetics and the Family*, i. 186-190.

Loeb, Leo. 1921. Inheritance of cancer in mice. *Amer. Nat.*, lv. 510-528.

Loeb, Leo. 1923. The inheritance of cancer in mice. *Eugenics, Genetics, and the Family*, i. 182-185.

Love, J. K. 1920. The origin of sporadic congenital deafness. *Journ. Laryngol., Rhinol., and Otol.*, xxxv. 263-270.

Lundborg, H. 1913. Medizinisch-biologische Familienforschungen innerhalb eines 2232-köpfigen Bauerngeschlechtes in Schweden (Provinz Blekinge). Jena: Fischer, 2 vols. Vol. i., pp. 519, 220; vol. 2, 10 pls., 52 charts.

Lundborg, H. 1920. Hereditary transmission of genotypical deaf-mutism. *Hereditas*, i. 35-40.

Lynch, Clara J. 1928. The inheritance of susceptibility to tar induced tumours in the lungs of mice. *Verh. V. Internat. Kongr. Vererb.*, ii. 1074-1080.

Lyon, Ernst. 1925. Elephantiasis auf erblicher Grundlage. *Zeit. f. Kinderheilk.*, xxxix. 36-43, fig. 1.

Macklin, M. T., and Bowman, J. Thornley. 1926. Inheritance of peroneal atrophy. *Journ. Amer. Med. Assoc.*, lxxxvi. 613-617, figs. 6.

MANSON, J. S. 1928. Observations on human heredity. London: Lewis, pp. 84, pls. 8, figs. 19.
MASON, R. 1926. Four generations of harelip. *Journ. Hered.*, xvii. 52.
MINKOWSKI, M., and SIDLER, A. 1928. Klinische und genealogische Untersuchungen zur Kenntnis der progressiven Muskeldystrophie. *Arch. J. Klaus-Stiftung*, iii. 239-298, figs. 11.
PARKER, G. 1928. A case of progressive muscular atrophy of the peroneal type. *Brit. Med. Journ.*, i. 1062-1063.
PEARL, R. 1928. Cancer from the viewpoint of the human biologist. *Internat. Clinics*, iii., series 38, 57-77, figs. 11.
PEARSON, K. 1907. A first study of the statistics of pulmonary tuberculosis. London: Dulau, pp. 26.
PREISER, E. A., and DAVENPORT, C. B. 1918. Multiple neurofibromatosis (von Recklinghausen's disease) and its inheritance: with description of a case. *Eug. Record. Office Bull.*, No. 19.
RIDDLE, OSCAR. 1918. A case of hereditary ataxia (?) in pigeons. *Proc. Soc. Exptl. Biol. and Med.*, xv. 56-57.
RISCHBIETH, H. Hare-lip and cleft palate. *Treas. Human Inheritance*, pt. iv. 79-123, pls. 8.
SEDGWICK, W. 1863. On the influence of sex in hereditary disease. *Brit. and Foreign Med.-Chirurg. Rev.*, xxxi. 445-478, xxxii. 159-197.
SLYE, MAUDE. 1926. The inheritance behaviour of cancer as a simple Mendelian recessive. Studies in the nature and inheritability of spontaneous cancer in mice. *Journ. Cancer Research*, x. 15-49, 15 charts.
STOCKS, PERCY. 1927. Fresh evidence of the inheritance factor in tuberculosis. *Ann. of Eugenics*, ii. 41-62, 84-95.
STOCKS, PERCY, and BARRINGTON, AMY. 1925. Hereditary disorders of bone development. *Treas. Human Inheritance*, vol. iii, pt. 1, pp. 182, pls. 9, figs. 210.
STRONG, L. C. 1926. Genetic studies on the nature of cancer. *Amer. Nat.*, lx. 201-233.
THOMPSON, J. W., MCBATTS, J., and DANFORTH, C. H. 1921. Hereditary and racial variation in the musculus palmaris longus. *Amer. Journ. Phys. Anthrop.*, iv. 205-218, figs. 3.
WEISS, F. 1929. Heredity in adherent tongue. *Journ. Hered.*, xx. 171-172.
WILSON, I. T. 1924. Two new hereditary tumours in Drosophila. *Genetics*, ix. 343-362, figs. 16.
WINDLE, B. C. A. 1891. Teratological evidence as to the heredity of acquired conditions. *Journ. Linn. Soc.*, xxiii. 448-502.
WRIGHT, SEWALL, and LEWIS, PAUL A. 1921. Factors in the resistance of guinea-pigs to tuberculosis, with special regard to inbreeding and heredity. *Amer. Nat.*, lv. 20-50.
YEARSLEY, MACLEOD. 1920. Can acquired deafness lead to congenital deafness? *Journ. Laryngol., Rhinol., and Otol.*, xxxv. 270-271.

CHAPTER XV

INHERITANCE OF MENTAL DIFFERENCES

When we consider mental traits, the evidence of inheritance in many cases appears sound and beyond dispute, although in the matter of human character it is less certain how far the accidents of early environment may suppress or seriously modify the expression of various inherited traits. Here we are in a region where the structural basis of the developed inheritance is so tenuous, and the contact with the environment so intimate —character and environment becoming so mutually involved and interpenetrating—that it is conceivable that the laws applying to structural characters are not applicable with the same rigidity to the elements or methods of reaction that go to make what we call human character. Nevertheless, critical students of the subject speak with one voice, and it is quite certain that heredity plays an equally important rôle here also. Indeed, the statistical results of Pearson (1904) indicate that for siblings the intensity of resemblance is as great for mental as for physical traits. He chose eight physical characters —namely, health, eye colour, hair colour, curliness of hair, cephalic index, head length, auricular height, and athletic power—and eight " mental " characters : vivacity, assertiveness, introspection, popularity, conscientiousness, temper, ability, and handwriting. While many of these characters are not definite enough for anything like accurate measurement, and therefore have no decisive value, yet the coefficient of correlation between brothers and sisters (siblings) comes out 0·51 for physical and 0·52 for mental characters. Schuster and Elderton (1907), from a statistical survey of Oxford class lists, attempted to determine the correlation in mental ability between father and son, and between brothers who attended the University. They found $r=0{\cdot}312$ for father and son, and $r=0{\cdot}405$ for brothers. They agree with Pearson that mental and physical characters are inherited with the same intensity.

Pearson has since (1919) considered the subject again from different data, comparing the results of applying the Binet-Simon test (*a*) to children in orphanages in California, hence under nearly uniform conditions; (*b*) to children in schools of Great Britain, under the greatest variety of conditions of education and home training. Although the mental environment was relatively uniform in one set of data and diversified in the other, yet the correlation of intelligence between siblings was the same in both groups, the resemblance, $r=0{\cdot}508$ in the Californian and $r=0{\cdot}515$ in the English data, indicating that heredity and not environment determined the differences in all cases.

But the situation as regards some psychical characteristics is beyond our present powers of accurate analysis. This is probably because we have not yet learned to define psychic characters in biological terms. That psychologists are beginning to recognise the necessity for an analysis of the mind from the point of view of the inheritance of mental traits, is shown particularly by McDougall's book, *Psychology, the Study of Behaviour* (*e.g.*, p. 187). In writing of the very close resemblances in intellect and character which twins often show, he says: "The more children are studied from this point of view, the more far-reaching does the influence of heredity appear." At the same time, he finds it impossible to define, except in the roughest way, the innate bases of these hereditary peculiarities. He concludes that we are compelled to believe they consist in "inherited mental structures of very considerable degrees of specialisation." McDougall points out that biologists and statisticians, in studying the inheritance of mental qualities, have frequently used crude and non-psychological popular distinctions, such as good temper, courage, conscientiousness, or popularity, and emphasises the need for accurate psychological analysis of the constitution of the mind as a basis for the study of mental inheritance. Biologists must undoubtedly look to psychologists for aid in this direction. In speaking of psychic characters we are not merely referring to the grosser mental differences, such as feeblemindedness and the presence or absence of musical, mathematical, or general ability, whose inheritance is almost universally admitted; but to the less readily definable traits which go to make up what we call temperament, disposition, and character. These have not yet received adequate biological classification, treating them as methods of reaction; but such a scheme, combined with

observations and comparison of the elements of human characters, would certainly help to clarify our conceptions concerning the basis of the differences involved.

Probably in individuals who are heterozygous for various character traits which are alternative in inheritance, either method may come into expression according to circumstances. And since every individual may be supposed to be heterozygous for many pairs of traits of human character, it appears possible that mental traits generally differ from structural characters in that, in the former, all the alternative possibilities may come into expression in the same individual at different times, thus adding to the complexity of the result. What we call human character in its developed form appears to consist in the acquired habit of inhibiting certain inherited tendencies, and giving free expression to others. But then, again, differences in powers of inhibition are undoubtedly inherited, and weakness in such powers may lead in the one extreme to vicious tendencies, and in the other to a free expression of the other elements of the inheritance. Nevertheless, there is always a choice of ideals to be aimed at, and it is necessary to distinguish in conduct between those who fail to reach their ideals and those who deliberately pursue non-moral ends.

The lay mind frequently goes astray on the question of the inheritance of ability by assuming that if the sons of an able father do not themselves show ability, this is a case of "failure of inheritance." In a scientific view of inheritance in such a case, one of the alternative factors has been inherited instead of that which conditions ability—an undesirable instead of a desirable quality has been handed on—or at least one of the necessary elements for the expression of ability is missing. In types of ability where the correlated action of several independent qualities or factors is required, the appearance of the same combination of exceptional qualities in the offspring is very likely to be infrequent, because of the presence of alternative characters in the germ plasm.

That the tendency to perform certain tricks when in a particular frame of mind may be inherited, was shown in a case cited by Darwin (*Animals and Plants*, chap. xii.) of a man who, as a boy, had the habit, when pleased, "of rapidly moving his fingers parallel to each other, and, when much excited, of raising both hands, with the fingers still moving, to the sides of his face on a level with the eyes." As a grown man the trick was with difficulty suppressed, but one of his eight children, a girl of

four and a half years, had exactly the same trick. Darwin states that imitation was out of the question.

A question which has been much disputed concerns the existence or non-existence of mental differences between human races. If such differences exist they must be inherited unless they are entirely produced by the environment. Davenport (1929) has brought forward cogent evidence to prove not only that definite differences in mental capacity exist between the negro and the white race, but that these differences are inherited in racial crosses. He points out that the races of dogs show constitutional hereditary differences in mental capacity, so that fox terriers are easily trained to catch rats, collies to herd sheep, pointers to flush game, etc. These differences in training ability depend on inherited differences in mental make-up.

That similar differences exist in mankind is indicated, for instance, by the occurrence of the mental conditions known as amok and latta in the Malay but not in other races. Davenport has answered this question by a series of experiments carried out on whites and blacks in Jamaica—experiments which are free from the objections usually urged against work of this kind. Most of the individuals belonged to a farming population, all spoke English, and the negroes were rather better educated than the whites. The latter were partly of German and partly of English descent.

Fifty to eighty adults of each racial group were studied by Dr. Steggerda as well as 50 to 100 children of ten to thirteen years of age. The tests were designed to determine the sensory and intellectual capacities of the two groups. The Seashore test of time discrimination was first applied, in which three notes are sounded on a gramophone record at slightly different intervals. Powers of discriminating slight differences in time probably depend on the anatomical structure of the ear, and are only slightly improved by training. The adults as a whole were better than the children in detecting time differences, and the negroes were better than the whites. Similarly, negroes were found to have a far better sense of rhythm than whites of corresponding age.

In a test of ability to copy three geometrical figures—a circle, a diamond, and a square—the whites were superior, as they were in drawing a man without any model and in reconstructing a manikin from six wooden pieces. These tests indicated greater ability to visualise properly and to work critically. In various other tests, including the form-board (Knox moron test), the

criticism of absurd sentences, and the Army Alpha tests, involving imagery, organisation, and common sense, the whites were superior. The result, that innate sensory and intellectual differences exist between the races, is thus definitely confirmed.

FEEBLEMINDEDNESS.

Considering now the inheritance of various forms of mentality, Galton (1869), in his classical work, *Hereditary Genius*, first dealt with the inheritance of mathematical and various other forms of ability. This and the subsequent studies are too well known to require treatment here. Hurst first pointed out the probability that musical ability was a Mendelian recessive. The same is apparently true of feeblemindedness, at least in its extreme form, two feebleminded parents almost invariably having only feebleminded children. The exceptions to the rule are probably explainable by illegitimacy. The literature of feeblemindedness is too well known and too extensive for full discussion, but reference may be made to some of the results. For the Mendelian interpretation Goddard (1912, 1914) and Estabrook (1916) may be cited.

Goddard (1914) finds that at least 50 per cent. of the paupers cared for in American institutions are FEEBLEMINDED, and at least 50 per cent. of the prostitutes are estimated to be in the same condition. Many criminals come in the same class, and there is also a close relation between feeblemindedness and alcoholism. On the basis of graded mental tests of the Binet-Simon Measuring Scale of Intelligence, individuals are classed as idiots when their mental age is 1-2 years, imbecile when it is 3-7 years, and morons when it is 8-12 years. The latter would be called feebleminded in England. The mental development may stop at any age, and feeblemindedness is essentially a condition of early suspension of mental development. Various accidents and certain diseases in childhood may result in feeblemindedness, but it would appear that the great majority of cases are hereditary. In hereditary feeblemindedness the children tend to have about the same grade of mentality as the parents. Sometimes accidents in childhood reduce an hereditary moron to imbecility or idiocy. When their mentality is under five years, individuals rarely become parents, but parenthood with a mental age of seven or eight is common.

The training in institutions for the mentally deficient shows

that it is impossible to develop a mind beyond its inherited capacity. The mental development may stop at any point, and training cannot push it any further, although the most patient and persistent efforts are made in this direction. When mental progress ceases, it is necessary to turn to manual training for any further development of the individual.

As regards inheritance, Goddard cites 42 matings, NF ♀ × FF ♂—*i.e.*, a heterozygous but normal mother and a feebleminded father—producing 144 children whose mentality is known. Of these, 71 were feebleminded and 73 normal, almost exactly in accord with the Mendelian expectation of equality. On the other hand, from matings FF ♀ × NF ♂ there were 193 children whose mentality is known, and they were 122 feebleminded to 71 normal. Hence it appears that the number of feebleminded considerably exceeds expectation when the mother is feebleminded. Again, in NF × NF matings (26) there were 185 offspring, and the mentality of 122 was determined, 83 being normal to 39 feebleminded (expectation for one Mendelian difference, 91·5 : 30·5). Among 476 children from FF × FF matings, only 6 are recorded as normal, and these were no doubt border-line cases, or perhaps illegitimate. Hence the evidence clearly favours the interpretation of feeblemindedness as a simple recessive.

Holmes (1921) and other writers are less willing to grant this conclusion, and the forms of feeblemindedness are undoubtedly more varied than was formerly realised. Holmes agrees with Pearson and Heron that feeblemindedness varies continuously, but he admits that this does not imply " that the various kinds of mental defect are not transmitted according to Mendel's law." He nevertheless concludes (p. 39) : " I very much doubt if the facts concerning the inheritance of mental defect are as yet known with sufficient precision to warrant our trying to force them into simple Mendelian formulæ." We cannot agree with his statement that "it seems improbable *a priori* that the inheritance of general mental development would follow the simple Mendelian formula for the inheritance of two contrasted characters." All sorts of physical defects in man and other animals, and in plants, are known to follow the behaviour of a simple recessive character. This appears to be due in each case to the fact that an altered element (gene) is present in a particular locus of a chromosome, and we find no difficulty in applying the same view to mental defects, which must have a physical basis.

We may, however, point out an inference which follows, and has not yet been generally recognised. If feeblemindedness is inherited as a Mendelian recessive, this in itself furnishes evidence that it has arisen as a defect mutation from the normal condition. On the whole, it appears most likely that feeblemindedness has arisen many times, and may still arise, as a defect mutation in various stocks, and although the condition itself may resemble in some respects the mental condition of primitive man, yet there appear to be important differences. Goddard cites a family of eleven feebleminded children from two white feebleminded parents. There were also two "normal" children, but they were black. The mentality of the negro is distinct from that of the feebleminded. The latter presumably occur also in primitive races. The evidence, so far as it goes, also appears to indicate the gradual evolution of the mentality of normal civilised man, involving many steps, whatever may have been the forces involved.

Holmes points out that where a normal person married to a feebleminded one has some feebleminded children, it is too easily assumed that the normal parent was heterozygous for this defect. If this were always true, it would give a very high frequency for the occurrence of this latent defect. It seems much more likely, as Holmes points out, that the normal mentality shows variable or incomplete dominance, especially when, as is usual in such matings, the normal parent is also intellectually below par.

Goddard estimated the number of feebleminded in the United States at 300,000 to 400,000. He thinks it important that the public should understand the mentality of a moron (mental age ten), and employ him accordingly, recognising his limitations. The moron has a lifetime in which to learn to do efficiently things that can be done by a boy of ten. Goddard suggests that their training should be carefully arranged according to mental age tests, that as many as possible should be "colonised," some sterilised, but the great mass "educated" for their proper work.

As an example of one type of feebleminded, Fig. 69 represents two mental and physical defectives from an Institution near London. Their ages were twenty-one and twenty-two years, but their mentality was that of a child of eight and, except for marks of greater age in their faces, they might have passed for boys of that age. They were treated intermittently with thyroid after their admission to the Institution at the age

of about nine years. Their weight and height have remained practically unaltered, nor was there any advancement in their intelligence. When the thyroid is increased, their features become sharper and they become more active mentally and physically. *Their appetites also increased, but their growth* and weight remain unaffected.

The "MONGOLIAN" is a well-defined type of mental defectiveness, which has generally been regarded as non-inherited. The oblique eyes and round faces of Asiatics are

FIG. 69.—TWO FEEBLE-MINDED CRETINS, AGE TWENTY-TWO AND TWENTY-ONE, FROM THE DARENTH COLONY, DARTFORD.

combined with short stubby fingers, rather dry rough skin, poor circulation, lack of occipital prominence, and usually in older cases a deeply furrowed tongue. The mentality is nearly always that of a four-year-old child. Mongolians usually appear in good-class families, they are not associated with feeblemindedness, and are frequently the last born in large families. They probably result from derangement of function (uterine exhaustion) leading to arrest of development, beginning at a definite point in the prenatal development. The causation of the type according to Goddard (1914) appears to be

purely physiological, without any element of inheritance. Probably defects of certain internal secretions are involved. It has been claimed, however, that there is some reason for regarding Mongolianism as a recessive Mendelian trait (see Davenport, 1920). There is evidence also that idiocy frequently results from a severe infection, from cerebro-spinal meningitis, or from syphilis, alcoholism, or addiction to drugs on the part of the parents. But, according to Davenport, statistics show that the great mass of idiots arise from feebleminded parents.

Ordahl (1927) tabulates the data from 159 families in which Mongolism occurs, and confirms the belief that it tends to appear in the children born late in large families, or when the mother is nearing the end of the child-bearing period. On the other hand, Chown (1927) describes a case of Mongolian idiocy in one of male twins and concludes that it must be due to a recessive gene.

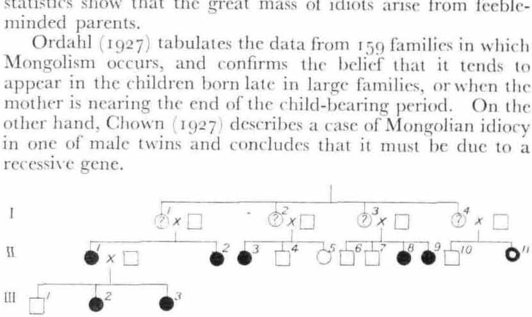


FIG. 70.—HEREDITARY IMBECILITY IN THE FEMALE LINE.

We have already seen that feeblemindedness is essentially a condition of arrested mental development. Epilepsy is a closely related neuropathic condition. Insanity is more variable in its causes, and is, like epilepsy, not always inheritable. Many data on the inheritance of mental defects are given by Guyer (1916).

The relations between feeblemindedness and insanity have frequently been misunderstood. From the point of view of the Binet-Simon tests, while feeblemindedness gives general arrested development at a certain level, insanity and epilepsy show "scattering" in the tests—*i.e.*, in the diseased brain some questions in various years will be missed. "Scattering" in tests of the feebleminded indicates the oncoming of insanity, which may not become evident for several years. In many respects feeblemindedness and insanity are at opposite ends of the mental scale, although an unusually high percentage of feebleminded become insane. Psychiatrists maintain that

insanity comes in highly developed nervous systems, which are easily thrown into an abnormal condition. Morons, on the other hand, represent often a vigorous organism of low intellect and strong physique. They often have exceptional strength, but cannot show it on a dynamometer because of lack of will power. They represent a more primitive type, with dullness to pain, etc., but under exceptional conditions they may perform surprising feats of strength.

Sedgwick (1861, 1863) records many instances of the inheritance of insane diatheses. In one family (Fig. 70) hereditary imbecility appears in nearly all the females of two generations, while the sons were normal No. II. 3 was eccentric and silly, while No. II. 11, though not an imbecile, was a religious fanatic and became a Mormon.

Inspection of charts does not convince one that insanity in the ancestry has any potent influence towards causing feeblemindedness. On the other hand, the feebleminded not infrequently have insane offspring. Insanity is a symptom of nervous derangement which will occasionally give rise to feeblemindedness. Thus, Goddard cites the case of Nora T., age thirteen years, mentality three. Her father and mother were both normal, but the feeblemindedness in the father's family and the insanity in the mother's family apparently brought about the result in Nora. Again, Bessie X. has a cousin who is epileptic and a number of distant relatives who are insane or epileptic, while others are " queer " or " peculiar." She is fifteen, with a mentality of two, and her condition is looked upon as a summing-up of various morbid tendencies which have appeared sporadically in several generations of her ancestors.

While feeblemindedness is certainly far removed from genius in the mental scale, representing a primitive undeveloped mental condition, it is often but a step from insanity to genius. Indeed, many geniuses would pass with any psychiatrist as true insanities. The diagnosis may depend on whether the aberration is useful or dangerous. But it is impossible to graft genius on to feeblemindedness, and the loss of a whole feebleminded stock would not involve the suppression of a single genius. For in feebleminded families even the " normals " are usually of low-grade intelligence, and they are as a rule correspondingly low in social grade. Notwithstanding this, it is clear that the condition of the feebleminded does not result from their environment, but rather that their lack of capacity

causes them to gravitate into squalid conditions, since they cannot grapple adequately with the complexities and subtleties of modern civilised life.

INSANITY.

Urquhart (1909) classifies insanity as melancholia, mania or dementia which are acquired, and idiocy and imbecility which are congenital. The latter conditions are, usually at least, accompanied by gross physical deficiencies. The pedigrees of insanity are usually unsatisfactory in failing to distinguish between different types, and so they give no general rule of inheritance, although many of them run through three generations.

Meyerson (1923) classifies psychoses in the following manner: (1) Paranoid psychosis, which will give paranoia or dementia præcox in the descendants; (2) dementia præcox, which gives usually the same condition, but also feebleminded and sometimes epilepsy; (3) manic-depressive insanity, which gives the same condition, or dementia præcox; (4) involution psychosis, which is always followed by dementia præcox in the descendants; (5) senile psychosis, which in later generations may give all types, including dementia præcox, manic-depressives, paranoids, imbecility and epilepsy.

Rosanoff (1923) also makes a classification of mental disorders. He points out that these conditions frequently skip one or more generations, suggesting a recessive inheritance, and that members of the same family do not necessarily suffer from the same clinical form of mental disorder. He also points out that while manic-depressive ancestors may have descendants with dementia præcox, the reverse is very rarely the case. He therefore arranges the various psychopathic conditions in a descending scale of recessiveness, as follows: normal, manic - depressive psychoses, dementia præcox, epilepsy.

Holmes (1921) has pointed out that the germplasm of neurotic stocks may be affected in a variety of ways in different individuals. He says (p. 49): " Charts of the inheritance of insanity show that the afflicted individuals exhibit a great diversity of symptoms in successive generations." Particular types of insanity, however, tend to run in certain families. This is particularly true of dementia præcox (see p. 278) and periodical insanity. Unlike most forms of insanity, HUNTINGDON'S

CHOREA appears to be usually a typical dominant character in inheritance.

This disease was described by Dr. Huntingdon in 1872. Davenport (1915) published four large pedigrees of this condition in families on Long Island (Connecticut) and Eastern Massachusetts, all descended from six persons who emigrated to America in the seventeenth century. Although three of them were probably brothers, yet four different biotypes of the disease are represented. In these families nearly 1,000 cases of chorea are included. Huntingdon's chorea is characterised by (1) persistent tremors of the head, appendages, and trunk; (2) the onset of such tremors in middle or late life; (3) their progressive nature, and (4) progressive mental deterioration, ending with dementia and suicidal tendencies. In one biotype, tremor was absent, in another there were tremors without mental deterioration, in a third the chorea does not progress, and in the fourth the onset of choreic symptoms is early in life. Thus the symptoms differ from strain to strain, but there is also intermingling of strains by marriage.

Apparently the "law of anticipation" is followed, but this is partly or wholly illusory because the grandfathers are selected (the onset was at least late enough for them to become parents) while the grandchildren include those in whom the onset is so early that they will never marry. Among the 3,000 relatives of the choreics, many nervous traits are found, including 39 cases of epilepsy, 19 of infantile convulsions, 41 of hydrocephaly and 73 feebleminded. Hence chorea occurs in families with general liability to mental and nervous troubles. There is no evidence that the presence of these nervous conditions affects the marriage rate.

Entres (1921) has collected material from 15 families confirming that Huntingdon's chorea is dominant in inheritance. Clarke and MacArthur (1924) have traced another family, descended from an immigrant to Canada from England early in the nineteenth century. His descendants have spread into various Provinces and American States. The choreics all married normals and their children in the second and third generations numbered 33 choreics : 12 normal, or 3 : 1. This ratio instead of 1 : 1 clearly suggests that in this pedigree two independent dominant factors for chorea are present. In some other pedigrees the ratio appears to be 1 : 1, indicating a single factor present. A man in the third generation murdered his infant child and this led to investigation of his pedigree. Eleven

choreic insane were found to be in asylums. Obviously those who are liable to show chorea in middle age should not marry.

Kehrer (1928), in a study of chorea, myoclony, and athetosis, emphasises the view that diseases of the central nervous system only belong to types and are not fixed units so far as heredity is concerned. The aim should not be merely to show that Mendelian laws hold or do not hold in nervous pathology, but to construct a symptomatic-genealogical structure analysis which will form the basis of a natural system of hereditary types in neurology. The multiform causal forces at work are like a series of parallelograms in every individual case. From the picture of symptoms must be discovered the basis of the phenomena and from that the fundamental genetic and environmental causes. The causes of minor chorea are exclusively constitutional or hereditary. When choreatic symptoms and progressive paralysis appear in the same individual either simultaneously or successively, they are probably usually of independent origin in the bearer.

As regards the relations between myoclony and epilepsy, Kehrer thinks that notwithstanding the work of Lundborg the question of hereditary coupling between the two is not yet clear. In a family, some will have one, some the other, and some both. This suggests linkage with crossing over. Kehrer identifies three new types of Huntingdon's chorea: (1) Constitutional chorea without choreopathic temperament or with choreic temperament alone, or with choreic (paranoid) psychosis with or without progressive dementia; (2) tremor and either constitutional—*i.e.* psychic-reactive—or progressive (senile or climacteric), universal, or regional chorea; (3) choreopathic temperament, chorea dementia, or choreic movements. Four other types are also distinguished. It is not clear how imbecility is to be considered in a pedigree of Huntingdon's chorea. Many pedigrees of chorea are given. Two features of them are a high infant death-rate and the common occurrence of twins.

C. and O. Vogt (1922) point out many structural pathological conditions in the brain and central nervous system accompanying various nervous diseases, including chorea, Huntingdon's chorea, and athetosis.

Dipsomania, or a morbid craving for alcohol, has been studied in an extensive pedigree (Fig. 71) by Kroon (1924). He regards it as a sex-linked factor, dominant in males and recessive in females, like the horns in some breeds of sheep.

Although only males exhibit it, both males and females may transmit it. If germinally determined, it must then be represented in an autosome. Kroon explains the reversal of dominance by the presence of a female-sex-limited inhibiting factor. In the pedigree, II. 8 was a drunkard. His mother and sister must have been transmitters. In this type of inheritance, if a normal man married a heterozygous (carrier) woman, then *half* the sons would be dipsomaniacs and *half* the daughters would be carriers.

While the feebleminded may be considered to form a graded series, insanity is much more varied in its manifestations, and is to be regarded as a pathological condition working havoc with the normal mental mechanism, rather than a simple defect of mental machinery. Some types of insanity may only appear late in life and yet are inherited, showing that the seeds of ultimate derangement are present in the germplasm. In other cases, an exceptional mental or physical strain may bring out phenomena of insanity which would never appear under ordinary circumstances.

Ordahl (1919) made a study of fifty families in California containing feeblemindedness. He concludes that the parents of the feebleminded are often borderline cases and escape detection by ordinary means. Seventy-two per cent. of the fifty families showed defective inheritance. Of the living children, 5·6 per cent. were idiots, 15·6 per cent. imbeciles, 26·2 per cent. morons, 3·1 per cent. dull normal, 1·2 per cent. psychopathic, 48·1 per cent. normal. Ordahl believes that the moron and dull normal can be detected by expert means in the early school years. Otis (1916) aims to reconcile the views of Pearson and Davenport. He considers it important to distinguish between intelligence and "brightness"—*i.e.*, the degree the child is in advance of the normal development of intelligence. Pearson showed that all degrees of intelligence (meaning brightness) exist, but this does not exclude the Mendelian inheritance of any degree when mated with feeblemindedness. Otis concludes that "the existence of all grades of brightness, and the possibility of the universal Mendelian inheritance of different grades of brightness, are therefore seen to be entirely compatible." This is in accord with much other Mendelian behaviour.

It is recognised that EPILEPSY occurs in a great variety of forms, and the pedigrees studied by Davenport and Weeks and others indicate that the common form at any rate is

recessive. A relation between epilepsy and feeblemindedness is also indicated, such that if one parent is epileptic and the other feebleminded, all the children will be either epileptic or feebleminded.

Brain (1926) studied 200 epileptics and found a family history in 28 per cent. of them. A family history is more

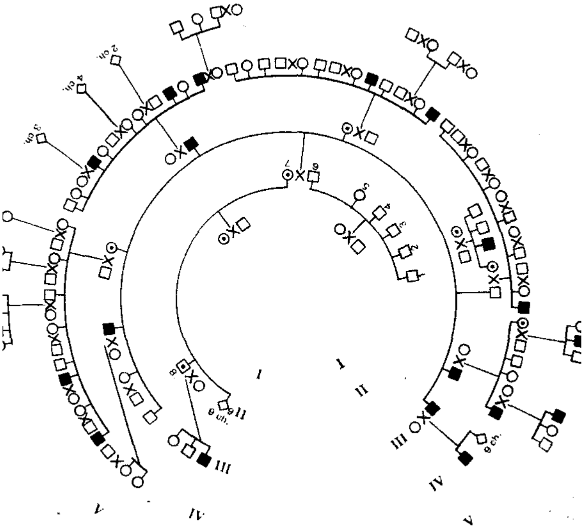


FIG. 71.—PEDIGREE OF DIPSOMANIA. (After Kroon.)

frequent in females than in males, and the onset occurs in the first decade of life more often in those with a family history. Epileptics are found to transmit the disease to about one in twenty of their offspring. There is a higher proportion of epileptics among first-born, probably owing to cerebral injury at birth. It is found to be impossible to distinguish trauma effects from inherited epilepsy. Hence there are great difficulties in determining the manner of inheritance, because the

inherited cannot be distinguished from the non-inherited form. Davenport and Weeks combined a variety of conditions in their studies. Brain found one case in which both parents had epilepsy as well as the paternal grandmother and the paternal uncle; yet all the four children of this marriage were normal. Probably in this case the mother's epilepsy was due to trauma and not inherited. Ganter (1927) gives many pedigrees, but most of them too short to be of much value. He concludes that epilepsy is transmitted by father to son and by mother to son and daughter. Alcoholism is also believed to increase its incidence, though it is doubtful here which is cause and which effect.

Timme (1924), in a discussion of the nature of the hereditary units in hereditary disturbances of the nervous system, points out that in epileptics the blood sugar is below normal before epileptic attacks, and also preceding the attack of certain types of migraine. He thinks that epilepsy, excessive growth, migraine and blood-sugar disturbance are all interrelated, and that there must be an underlying hereditary factor. Muscular dystrophy or wasting is also probably due to a combination of several factors.

Rosett (1929), in a recent paper, takes a somewhat different view. He has made cinematographic studies of epileptic seizures and concludes that epilepsy is a form of the tetanic state which has its origin in an inhibition of the sensory system, which results in a release of muscular activity. Epileptic seizure differs from normal activity in increased facility and a greater degree of nerve inhibition. Rosett considers it is impossible to prove the inheritance of a defective nervous system as such in epileptic cases. Generation after generation of epileptics may have a defect consisting either in a disproportion between the child's head and the mother's pelvis, or of a defective correspondence between the special metabolism of pregnancy and the embryonic formation of the brain. Even when epilepsy is apparently inherited from the father, it is unsafe, he thinks, to conclude that a defective brain is inherited rather than a metabolic defect which by its action on the brain causes epilepsy in both parent and child.

Various investigations indicate (Davenport, 1920) that DEMENTIA PRÆCOX* may be a Mendelian recessive. Rüdin (1916) finds that various other psychoses accompany dementia

* Adolescent insanity marked by melancholia and other emotional states.

præcox, and thinks that a Mendelian explanation is possible. Hoffman (1921), in a study of dementia præcox and the manic depressive condition, concludes that two factors are involved in the former, while in the latter a dominant character in some form is concerned.

Sir Frederick Mott (1922) discusses the origin of dementia præcox. He shows that in dementia præcox, congenital imbecility and various other psychoses there is a definite tendency to failure of development of the Graafian follicles. The few that develop show deficiency of chromatin and, as in the male, where there is a complete arrest of spermatogenesis in dementia præcox, there is a failure of the reduction divisions. In the nervous system of cases of dementia præcox there are widespread morbid changes in the nucleus and cytoplasm of the neurones. This is most marked in the cortex cerebri. The nuclei are swollen and irregular, with a change in staining reaction from basophile to eosinophile. There is also a deficiency of Nissl's granules, an excess of lipoid granules and the cytoplasm is acidophile. These various changes in the cells of the cortex cerebri, the ovaries, and testes are best explained as the result of a germinal biochemical deficiency.

Hansen (1922) describes a pedigree from the Royal House of Hanover, descended from the insane Duke William the Pious, who doubtless suffered from dementia præcox and had some insane descendants. Retinitis pigmentosa frequently occurs in the same family with dementia præcox and imbecility. The conclusion reached is that dementia præcox is polyhybrid, depending on at least two co-operating factors, one of which is a dominant common factor, the other a recessive special factor. M. Müller (1926) gives pedigrees of a schizophrenic father (with dementia præcox) and a schizoid mother, who married and had three daughters, all schizophrenic. In the two families thus brought together the condition is inherited as a dominant, with variations in its psychopathic expression.

Hoffman (1926), from a consideration of several hundred pedigrees collected by E. Rüdin, concludes that dementia præcox develops in those who have shown a schizoid temperament and whose parents have shown the same. It is believed to depend on primitive action patterns present in every one, recalling the child and the savage. They find expression only in those inheriting this temperament, which tends to go with the asthenic constitution—tall and slender build. Inherited

factors which influence the endocrine glands may tend to determine both the constitution and the temperament.

AMAUROTIC IDIOCY, already referred to under ocular defects (see p. 88), is sometimes known as Tay-Sachs disease. It was first described by Waren Tay in 1881. The classical R—— family was described by Kingdon and Russell (1897), who called it *infantile cerebral degeneration with symmetrical changes at the macula.* Two normal strong and unrelated German Jews had seven children, five of whom (four boys and a girl) were afflicted and died. The parents of the father were cousins. Stewart (1929) has recently studied the later history of this family at the Hull Hospital. The completed family from the above two parents numbered 12, the later children being all normal with the somewhat doubtful exception of one. The numbers in this family may then be taken as six amaurotic : six normal or 5 : 7. A normal daughter has since had two children, one of whom (a girl) died of amaurosis. The evidence indicates that the inheritance is recessive.

PEDIGREES OF DEGENERACY.

Various families characterised by defective mentality and anti-social conduct through many generations have been the subject of study from an inheritance point of view. In America there have been the Jukes in New York, the Kallikaks in New Jersey, the Hill Folk, the Nam family, the tribe of Ishmael in Indiana and the Win tribe in Virginia, in Switzerland the Zeros.

That even the most degraded family is not entirely incapable of better things in any of its members is shown by the later history of the Juke family (Estabrook, 1916), whose history has been a continuous record of crime, vice, and feeblemindedness. It dates from 1720-40, and has been an untold burden upon the State. Dugdale published a history of it in 1877. Estabrook shows that, in their history, out of 399 fertile marriages about 176 might be classed as eugenic matings and 223 as cacogenic. Fifty-five per cent. of these matings should have been prevented, even putting the eugenic standard as regards intelligence very low. Had this taken place, the remainder would now show less than 5 per cent. of offspring with undesirable traits. As it is, over half the total offspring are mentally defective or have antisocial traits. The occurrence of both desirable and undesirable individuals in the same sibship is often startlingly clear in these families.

A study of a Pennsylvania family containing good and bad elements has been made by Miss Key (1920, 1923). Two pioneer families of German descent are traced through five and six generations on American soil. They mostly belong to the great middle class, containing no eminent members and no notorious criminals. The study began with four young feebleminded in a Pennsylvania Institution. The history of this family, with a network of descent including 1,822 individuals, shows the establishment of lines which vary greatly in social efficiency. Marriage selection has given rise to three strongly contrasting lines, the original defects persisting or becoming accentuated in some lines, while marriage into better strains has produced other lines socially more efficient. One family began with a German and his wife, who immigrated into Western Pennsylvania in the latter part of the eighteenth century. He was a fair specimen of the pioneer type, but his wife was totally lacking in any sense of number or quantity, and could neither sew, spin, nor weave acceptably. They had children, three of whom were apparently feebleminded, while the others, through marriages with different types, established various lines, some of which split up into divergent branches. Five separate strains are traced in this family. Another German immigrant and his wife, about the same time, had twelve children. They were very tall and possessed great strength, qualities which some of their descendants perpetuated. Six of the children formed socially efficient strains, four died without marrying, while two daughters, the dullest and slowest of the fraternity, but with great strength and endurance, married into defective stock belonging to the previous family, and gave rise to an undesirable strain.

The characteristics of the various lines are determined by the combination of traits carried by their founders, together with the leading traits of the strains into which they married. There is a sifting out in every generation. Where weakness marries strength the defect may appear, but in lessened degree. This results in the practical elimination of some defects (in their external expression), and in increased efficiency. The intermarriages of defectives, on the other hand, give a continuous line of defectives requiring institutional care. Two of the lines continue to be mixed, showing defectives, degenerates, and socially fit. The degenerate branches gravitate downwards, and produce nothing but degeneracy. The rapid multiplication of these people is most serious. Miss Key points out that

public opinion is helpless to prevent marriages between them, and suggests State control of marriages through a State Eugenics Board, with power to prohibit certain unions under penalty after studying the hereditary defects of the proposed parties to a marriage. But it is not to be expected that a ban on marriage would prevent people of this type from reproducing themselves. It is noticeable that while defective members of these stocks remain for the most part within a few miles of their place of origin, and hence tend to establish a defective group in the community, the better members, by marriage or otherwise, remove to greater distances and a new environment.

Estabrook (1923) has described the "Ishmaelites." They are descended from about 400 interrelated families in the pauper population of Indianapolis, who were stranded here during the movement westwards. They were shiftless men who begged and wandered in the summer, returning to the city to be supported by public charity in the winter. One of the progenitors was John Ishmael, who married a half-breed woman and came to Indiana about 1840. They and their descendants were wanderers, licentious, mentally weak, and unfit for hard work. By 1885 they numbered 6,000, in 1921 not less than 10,000, found mainly scattered over Indiana, Kentucky, Illinois, Ohio, Michigan, Iowa, and Kansas. Probably many are descendants of men and women deported from England to Virginia in 1692-1770. They are expert beggars, have an illegitimacy rate higher than the Jukes or Nams, are known from their habits as American gipsies, and they continue to spread.

A similar study of the Wins of Virginia has been made by Estabrook and McDougle (1926). In an area of about eight miles by four is a community of about 500 people living mostly in shacks. They are descended from Indian-negro-white crosses, and have been living in the same locality for over a century. Their entire genealogy has been deciphered from county and State records. They start from three Indians and a white man. The latter married a half-breed Indian woman and had many children. A sister married an Indian, probably of mixed blood, in 1790. The son married a cousin, and from them half the Wins are descended. In later generations they intermarried with negroes. Some of the descendants have the physical traits of Indians, many show mixed Indian-negro-white characters with light skin and hair, some are copper colour and very dull, some vicious. The population is probably too much

mixed to be of much use in the study of physical inheritance in racial crosses.

The Zero family are described by Jörger (1905). His extensive study began in 1886 in Xand, a valley in Switzerland with 700-800 people. It forms an isolated oasis in geography, speech, religion, and politics. The people are very much inbred, and they are addicted to alcoholism, vagabondism, crime, immorality, feeblemindedness, and pauperism.

Temperaments.

Various attempts to analyse temperaments and their inheritance have been made, notably by Davenport (1915). He divides temperaments into hyperkinetic or nervous and hypokinetic or phlegmatic, and recognises two grades of each. A dualism of this kind, romantic and classic types, radical and conservative, feebly and strongly inhibited, he finds running through the whole population; also a tendency for matings to take place between unlike temperaments. He hypothecates a factor E producing periodic excitement, its absence *e* producing calmness. Another factor C makes for cheerfulness, while *c* permits more or less periodic depression; and he finds that C and E are independently inherited. As a modern attempt in the anatomy of melancholy, this shows courage in the effort to explore a field which is notoriously full of pitfalls. That it is inadequate as a complete analysis appears obvious. The desirability of creating "factors" for calmness and cheerfulness appears very doubtful.

Nomadism, or the wandering instinct, Davenport (1915) treats as a fundamental human instinct, which is typically inhibited in intelligent civilised adults. It appears to be a sex-linked recessive monohybrid trait. Sons are found to be nomadic only when their mothers belong to nomadic stock. Daughters are nomadic only when the mother belongs to such a stock and the father is also nomadic. The impulse occurs frequently in families showing such periodic behaviour as depression, migraine,* epilepsy, and hysteria. Nomadism would appear to be more widespread in the Anglo-Saxon population of North America than in the resident population of Britain. This is probably because emigration has always been more largely of the roving types, the more sedentary elements

* A nervous affection marked by periodic headache, often confined to one side of the head, and accompanied by nausea and other symptoms.

of the population preferring to remain behind. This difference probably applies chiefly to the labouring and agricultural classes, the higher classes being able to satisfy their nomadic instincts by travel.

Inherited mental differences appear to be determined by germinal changes affecting the structure of the nervous system or the biochemical character of the blood and other body fluids or tissues. Traced backwards in the ontogeny, they must have a purely physical basis like other germinal changes. The description of a breed of goats in Kentucky (Hooper, 1916) is instructive in this connection. When frightened, their fore legs become stiff, and they hop along, dragging their hind legs. If much frightened, the latter also become stiff, and the animal falls over. Such a breed must have arisen through a germinal change affecting chiefly the nervous system. A very similar condition appears in sheep, and also in horses and cattle, as a result of feeding too freely on pampas grass, *Poa argentina* (Jones and Arnold, 1917). But it is a form of intoxication, and is not inherited.

Paralysis agitans, or shaking palsy, was described by Parkinson in 1817. The individual shows tremulous motions and a tendency to pass from a walking to a running pace; while the senses and the intellect are uninjured, the facial muscles are characteristically rigid like a mask. Heredity is an ætiological factor in 10-15 per cent. of cases, according to Bell and Clark (1926), and the condition is associated with nervous degeneration in a neuropathic stock in 25-30 per cent. of cases. Hereditary cases tend to occur early in life, but palsy may be produced by trauma, emotional shock, overwork, infection, arteriosclerosis, etc. The pedigree of Bell and Clark shows palsy in two or three males, and three or four females in two generations. Seven other pedigrees are collected from the literature. In Clark's case the character appears to show dominance after its first appearance; in another pedigree it is clearly recessive, appearing in the children from several cousin marriages. It appears to be a dominant in the others. One of these is Günther's pedigree, in which the onset is early in life.

Cole (1920) describes in guinea-pigs a form of congenital palsy which is not exactly like any nervous disorder in man, though it resembles ataxia in pigeons, which Riddle finds is a recessive character with some irregularities in inheritance. Congenital palsy in guinea-pigs runs a brief course, ending in

death at an early age. The neurosis appeared in 1914, and is characterised by clonic spasms,* particularly of the legs, in which the animal lies helpless. It is inherited as a simple Mendelian recessive, heterozygotes being entirely normal. Hurst states that "feeblemindedness" in pigeons is a recessive. Tumbling in pigeons and "waltzing" in mice and rats (again recessive) are other examples of inherited nervous disorders in animals. These defects have been shown to be due to defective semicircular canals.

Facial spasm is inherited in a family described by Goldsmith (1927). It is never under control of the subject and occurs during sleeping or waking hours, being probably due to an irritant in the reflex spinal or bulbo-spinal arc. Stocks reports a Polish family in which 13 members were affected in four generations, and it skips two generations. In Goldsmith's family a point in the middle of the chin quivers (*a*) all the time or (*b*) only when the person is angry or excited. This is associated with high temperature and is recognised as characteristic of the family. In a pedigree of five generations, 79 individuals are affected and over 57 are known to be unaffected. A factor C is assumed, to account for the condition (*b*), and an intensifying factor T which causes high temper. A is a weaker dominant factor which only shows its effect in the presence of T. In how far this system of factors is justified remains to be seen.

Manson (1928) describes a family having *spastic paraplegia* with ataxia and mental defect. The three daughters and son were all affected, the parents normal. The first signs of the disease were at the age of seven or eight, when they were noticed to stagger in walking. The first daughter died at twenty-two, the son at twenty-seven; the other daughters are twenty-eight and twenty-three years old respectively. They have a vacant expression, slow and difficult speech, can answer simple questions, but cannot read. The mother's family was normal, the father's father was a chronic invalid in a workhouse infirmary. The condition is possibly a two-factor recessive, one factor inherited from each parent. Weissenberg (1927) notes a Jewish family in Tiflis with recessive spastic paraplegia; also hereditary tremor in a Jewish and a Russian family, inherited as a dominant in three generations; and a Jewish family with a torsion neurosis (recessive).

The inheritance of wildness in rats has already been referred to. Yerkes (1913) made a study of wild and tame rats and their

* Spasms in which rigidity and relaxation succeed each other.

F_1 and F_2 hybrids. He proved that wildness, savageness, and timidity are inherited, although wildness and timidity are very difficult to distinguish. Coburn (1922) has made a study of 1,300 mice, hybrids between wild and tame, in three generations. He made careful psychological tests of his animals, and concludes that the inheritance of wildness and savageness in mice is Mendelian of the "blending" or multiple factor type, but much more work is needed before the precise manner of inheritance can be stated. He thinks, however, that the two behaviour complexes, wildness and savageness, result from several different inheritance factors which appear to follow Mendelian rules.

Vicari (1923) studied the results of crossing Japanese waltzing mice with albinos. Both races had been inbred for many generations, and they ran the maze in much the same way. The F_1 was more vigorous than either parent, very quick and active like wild mice. Ten per cent. of them made more perfect trials in the maze than either parent, and in less time; 45 Japanese, 75 albinos, and 110 hybrids were tested. The hybrids also retained a formed habit better than either parent. The F_1 hybrids were thus different from either parent race, showing greater learning capacity and taking less time in the trials. This is regarded as a phenomenon of heterosis in hybrid behaviour traits, two mentally and physically mediocre races producing a superior F_1.

An attempt to analyse genetically the temperamental differences in rats has been made by Sadovnikova-Koltzova (1929), the method being by isolation and selective breeding to separate strains with different psychic qualities, and then by crossing to study the laws of their inheritance. In earlier work 123 rats were studied, mostly descended from a cross between a tame white rat and a wild male. In the present investigation, 445 rats descended from a half-wild male and a tame female of the previous pedigree have been studied by taking their performance in a labyrinth. Nearly a hundred rats descended from other crosses between wild and semi-wild or active and inactive parents have been tested. In general, it is found that male rats are more active than females. In crosses between wild and tame rats a series of intergrades is obtained, which are interpreted as due to several different genes for temperament, not neuro-psychic but chemico-psychic characters. The most important of these are regarded as (1) activity, (2) wildness and fear, (3) the searching instinct.

Much has been written on the inheritance of ABILITY in

man, but it is scarcely appropriate to include here. Reference will be made, however, to one work of fundamental bearing on the nature and inheritance of ability. Spearman (1927) has endeavoured to show, from a large body of work in experimental psychology, statistically treated, that in man there is a general intellectual factor, *g*, which is constant for the individual; and that in addition there are a number of special abilities or group factors. The best established of these are believed to be (1) some forms of memorising, (2) certain forms of fatigue, (3) musical ability, (4) logical relations, (5) arithmetical relations, (6) mechanical relations, (7) psychological relations. Such an analysis of the mind, if confirmed and carried further, might furnish the basis for an experimental psychological study of mental inheritance. At present, musical ability appears to be the only form of ability the manner of inheritance of which can be profitably discussed, although it can be recognised that many other forms of ability are clearly inherited.

Musical Ability.

That races differ in their musical aptitudes is generally recognised, and that musical ability "runs in families" is well known. The Bach family is, of course, the most exceptional, but innumerable other families show the inheritance of lesser degrees of musical ability. The Bachs were creative musicians, and the family begins with Hans Bach, born about 1520. His son Veit Bach loved and practised music. In the third generation there were two sons, Lips and Johannes, the latter being called the Spielmann. Of the five sons of Lips, one was a musician, another had a son a professional musician. Three of the five sons of Johannes were musicians. His second son had 24 descendants in three generations, eight of whom were musicians. The third son's children included John Sebastian Bach, who married first a member of the Bach family and afterwards a woman of another musical family. From this branch in four generations numbering 58 descendants, 22 were professional musicians. The fourth son of Johannes had 28 descendants in three generations, including 7 musicians. The fifth son was not a musician, nor were his three sons.

In eight generations of this remarkable family pedigree, including 136 persons (99 ♂, 37 ♀), 50 (all males) were musicians, and practically all were composers as well as performers. In the seventh generation 35 males are known, of whom 16

were musical. It is unfortunate that nothing is known of the musical ability of the women in this family.

Hurst first suggested that this characteristic was a Mendelian recessive. A study of five musical families by Drinkwater (1916) partly supports this conclusion. A family of organists was traced through several generations, and in every case where both parents were musical all the children showed musical ability. In another branch of this family, where both parents lack musical ability, all the children lack it. These families were united by marriage, but instead of all the children being non-musical, exactly 50 per cent. of them were musical, two being professionals of great ability. It therefore appears that musical ability may be a recessive which may nevertheless appear in some cases in the heterozygous condition. Artistic ability was also traced through four generations as a recessive character. But further evidence is required for clear conclusions regarding the manner of inheritance of musical and artistic ability.

Miss Stanton (1922) has made records of the musical capacities in various American families containing one or more distinguished musicians. The measures of musical capacity used were (1) sense of pitch, (2) sense of intensity, (3) sense of time, (4) tonal memory. These are believed from extensive experimentation to be basic qualities in connection with musical ability, being little affected by practice, age, musical training, sex, or general intelligence. Discrimination tests were made on the basis of phonographic records and standard laboratory apparatus, 531 individuals being classed as poor, average, superior, etc., on the basis of each test. As regards inheritance, the results are not extensive enough to warrant any very definite statement of laws. It is nevertheless suggested that the data indicate the dominance and segregation of superior capacity from average and poor capacities.

Parents who are musical and have a musical ancestry will have musical children, while the converse is also true, and one musical and one non-musical parent will have children of both types.

It is concluded that " the inheritance of musical capacities seems, indeed, to follow Mendelian principles, but the method of inheritance is so complex that it is impossible now to state how many factors may be present." It is doubtful if such a result has much value, beyond the recognition of the fact that degrees of musical capacity are probably inherited.

Haecker and Ziehen (1922) studied the inheritance of musical ability in several thousand persons where one parent was musical and the other was not. The boys were found to be more musical than the girls, especially if their mother was musical. Children of marked musical ability may show it before they are two years of age. Such children may sing correctly before they can talk. J. A. and F. Mjöen (1926), from a study of musical ability in Norway, find that ungifted parents never have very gifted children, while very gifted parents never have ungifted children. The higher the average gifts of the parents, the higher will be the average of the children. Great divergence of the parents in musical gifts has an unfavourable influence on the children's musical ability. Whether musical gifts are regarded as dominant, intermediate, or recessive will depend on where the line is drawn between "musical" and "unmusical," for there is no hard and fast line. Many details are discussed which cannot be entered into here.

Seashore (1923) endeavours by the methods of applied psychology to measure musical capacity rather than achievement. He makes an analysis of musical talent, in which 26 isolable factors which may be inherited are recognised. They include sensory, motor, representative, and general capacities, each being further divided—*e.g.*, sensory into discrimination of pitch, tone, and intensity. Sensory capacity for pitch is represented by measurements of sense of pitch in a simple tone, sense of timbre in a rich note, and sense of consonance in harmony. These all depend on the analysing power of the organ of Corti. The factors in musical ability are thus all psycho-physical in nature and may be regarded from either the mental or the physical point of view. Miss Stanton (1923) has continued the application of these methods, four of the Seashore tests being given to 85 members of six families, and qualitative information was obtained for 531 people. The results were arranged in pedigree form. Of 11 children of musical stock, all were musical except one who was abnormal. Of 25 children from non-musical stock, all were non-musical, and of 17 children from a musical × non-musical parent, six were very musical, eleven non-musical.

Mjöen (1926*c*) finds that powers of tone-discrimination are not altered by practice, and he believes that this power of discrimination may be regarded as a symptom of musical ability. More recently (1928) he concludes that musicalness is determined in grade and kind by the more or less marked develop-

ment of 20 characters, which correspond largely with those of Seashore. The study of the inheritance of musical ability thus appears to be swamped at present in the welter of components into which it has been analysed.

HANDWRITING.

Pearson treats handwriting as a mental characteristic. There is no doubt that it is an extraordinary index of human character, and can be used for an intimate analysis of the character by one who is expert in the comparison and analysis of different types of cheirography. There is nothing mystical in this relationship. The handwriting is an expression of one's manner of doing things. It may be neat or slovenly, run together or disconnected, large and showy or small and carefully formed, with long loops, precisely crossed t's, large capitals, long flourishes, etc. In the hands of an expert these, and many much more minute details, yield a remarkably accurate analysis of the character and capacities of the individual. The autograph is truly the product of the whole man.

The analysis of this relationship between character and handwriting, a relationship which extends to the minutest details, is worthy of scientific study. The mood of the individual, whether elated or suffering from depression, is also registered in the handwriting. The striking resemblances one sometimes sees in the handwriting of relatives is associated with inherited similarities in character. Identical twins, however, sometimes show fairly marked differences in handwriting. This subject of the handwriting of twins is worthy of further investigation. It should throw light on (1) the similarities between twins; (2) the limits of relation between handwriting and character.

LITERATURE

Bell, Julia, and Clark, A. J. 1926. A pedigree of paralysis agitans. *Ann. of Eugenics*, i. 455-462, fig. 1.

Brain, W. Russell. 1926. The inheritance of epilepsy. *Quart. Journ. Med.*, xix. 299-310.

Chown, Gordon. 1927. A case of Mongolian idiocy occurring in one of male twins. *Canad. Med. Assoc. Journ.*, xvii. 943-944, figs. 3.

Clarke, C. K., and MacArthur, J. W. 1924. Four generations of hereditary chorea. *Journ. Hered.*, xv. 303-306, fig. 1.

Coburn, C. A. 1922. Heredity of wildness and savageness in mice. *Behaviour Monographs*, iv., No. 5, pp. 71.

Cole, L. J. 1920. Inheritance of congenital palsy in guinea-pigs. *Amer. Nat.*, liv. 130-151, figs. 3.

Davenport, C. B. 1915. Huntingdon's chorea in relation to heredity and eugenics. *Proc. Nat. Acad. Sci.*, i. 283.

Davenport, C. B. 1918. Inheritance of temperament. Carnegie Publ., No. 236.

Davenport, C. B. 1920. Heredity of constitutional mental disorders. *Psych. Bull.*, xvii. 300-310.

Davenport, C. B. 1929. Do races differ in mental capacity? *Human Biology*, i. 70-89, figs. 10.

Drinkwater, H. 1916. Inheritance of artistic and musical ability. *Journ. Genetics*, v. 229-241.

Entres, J. L. 1921. Zur Klinik und Vererbung der Huntingdonsche chorea. Berlin: Springer, pp. 149.

Estabrook, A. H. 1916. The Jukes in 1915. *Carnegie Inst. Wash. Publ.*, No. 240, pp. 85.

Estabrook, A. H. 1923. The tribe of Ishmael. *Eugenics, Genetics and the Family*, i. 398-404.

Estabrook, A. H., and McDougle, I. E. 1926. Mongrel Virginians: The Win tribe. Baltimore: Williams and Wilkins, pp. 205, pls. 2.

Ganter, R. 1927. Über Erblichkeit bei der Epilepsie und dem Schwachsinn. *Arch. f. Psychiat.*, lxxxi. 395-430.

Goddard, H. H. 1912. The Kallikak family: A study in the heredity of feeblemindedness. New York: Macmillan.

Goddard, H. H. 1914. Feeblemindedness: Its causes and consequences. New York: Macmillan.

Goldsmith, J. B. 1927. The inheritance of "facial spasm." *Journ. Hered.*, xviii. 185-187, figs. 3.

Guyer, Michael F. 1916. Being well-born. Indianapolis: Bobbs-Merril, pp. 374, figs. 39.

Haecker, V., and Ziehen, Th. 1922. Zur Vererbung und Entwicklung der musikalischen Begabuug. Leipzig: Barth.

Hansen, Søren. 1922. Heredity in the case of dementia præcox and related diseases. *Hereditas*, iii. 114-124.

Hoffman, H. 1921. Die Nachkommenschaft bei endogenen Psychosen. Berlin: Springer, pp. 233, figs. 43.

Hoffman, H. 1926. Familienpsychosen im schizophrenen Erbkreis. *Abhand. Neur., Psychiatrie, Psych.*, xxxii. pp. 120.

Holmes, S. J. 1921. The trend of the race. London: Constable, pp. 396.

Hooper, J. J. 1916. A peculiar breed of goats. *Science*, xliii. 571.

Jones, F. S., and Arnold, J. F. 1917. Staggers in sheep in Patagonia *Journ. Exp. Med.*, xxvi. 805-823, pls. 4.

Jörger, J. 1905. Die Familie Zero. *Arch. f. Rassen. u. Gesells.-Biol.*, ii. 494-559.

Kehrer, F. 1928. Erblichkeit und Nervenleiden. I. Ursachen und Erblichkeitskreis von Chorea, Myoklonie und Athetose. Berlin: Springer, pp. 136, figs. 6.

Key, Wilhelmine E. 1920. Heredity and social fitness: A study of differential mating in a Pennsylvania family, *Carnegie Inst. Wash. Publ.*, No. 296, pp. 102.

Key, Wilhelmine E. 1923. Heritable factors in human fitness and their social control. *Eugenics, Genetics, and the Family*, i. 405-412.

KINGDON, E. C., and RUSSELL, J. S. RISIEN, 1897. Infantile cerebral degeneration with symmetrical changes at the macula. *Trans. Medico-Chirurg. Soc.*, lxxx. 87-115, pls. 4.

KOCH, H., and MJÖEN, F. 1926. Die Erblichkeit der Musikalität. *Zeits. f. Psychol.*, xcix. 16-73.

KROON, H. M. 1924. Die Erblichkeit der Trunksucht in der Familie X. *Genetica*, vi. 391-400.

MANSON, J. S. 1928. Observations on human heredity. London: Lewis, pp. 84, pls. 8, figs. 19.

MEYERSON, A. 1923. Inheritance of mental disease. *Eugenics, Genetics, and the Family*, i. 218-225.

MJÖEN, FRIDTJOF. 1926. Die Bedeutung der Tonhöhenunterschiedsempfindlichkeit für die Musikalität und ihr Verhalten bei der Vererbung. *Hereditas*, vii. 161-188, 37 tables.

MJÖEN, JON ALFRED. 1925. Zur Erbanalyse der Musikalischen Begabung. *Hereditas*, vii. 109-128, figs. 3, tables 7.

MJÖEN, JON ALFRED. 1926. Zur psychologischen Bestimmung der Musikalität. *Zeits. f. angew. Psychologie*, xxvii. 217-233.

MJÖEN, JON ALFRED. 1928. Die Bedeutung der Kollateralen für den Begabungsgrad der Kinder. *Verh. V. Internat. Kongr. Vererb.* ii. 1122-1135, figs. 9.

MOTT, FREDERICK. 1922. The genetic origin of dementia præcox. Libro en Honor de D. S. Ramón y Cajal, i. 73-92, figs. 9.

MÜLLER, MARGUERITE. 1926. Casuistischer Beitrag zum Erbgang der Schizophrenie. *Arch. d. Julius Klaus-Stiftung*, ii. 273-315, 2 pedigrees.

ORDAHL, G. 1927. Birth rank of Mongolians. *Journ. Hered.*, xviii. 429-431.

OTIS, ARTHUR S. 1916. Heredity and mental defect. *Journ. Delinquency*, May, July, pp. 87-100, 125-128.

PEARSON, K. 1904. On the inheritance of the mental and moral characters in man, and its comparison with the inheritance of the physical characters. *Biometrika*, iii. 131-190.

PEARSON, K. 1919. Inheritance of psychical characters. *Biometrika*, xii. 367-372.

ROSANOFF, A. J. 1923. Inheritance of mental disorders. *Eugenics, Genetics, and the Family*, i. 226-230.

ROSETT, J. 1929. The epileptic seizure. *Arch. of Neurol. and Psychiatry*, xxi. 731-794, figs. 15.

RÜDIN, 1916. Studien über Vererbung und Entstehung geistiger Störungen. I. Zur Vererbung und Neuentstehung der Dementia Præcox. Berlin: J. Springer, pp. 172, figs. 66.

SADOVNIKOVA-KOLTZOVA, M.P. 1929. Genetische Analyse der Temperamentes der Ratten. *Zeits. f. ind. Abst. u. Vererb.*, xlix. 131-145, figs. 4.

SEASHORE, C. E. 1923. Individual and racial inheritance of musical traits. *Eugenics, Genetics, and the Family*, i. 231-238.

SEDGWICK, W. 1861. On sexual limitation in hereditary disease. *Brit. and Foreign Med.-Chirurg. Rev.*, xxvii. 477-489, xxviii. 198-214.

SEDGWICK, W. 1863. On the influence of sex in hereditary disease. *Brit. and Foreign Med.-Chirurg. Rev.*, xxxi. 445-478, xxxii. 159-197.

SCHUSTER, EDGAR, and ELDERTON, ETHEL. 1907. The inheritance of mental ability. *Galton Laboratory Memoirs*, 1.

SPEARMAN, C. 1927. The abilities of man: their nature and measurement. London: Macmillan, pp. 415.

STANTON, HAZEL M. 1922. Inheritance of specific musical capacities *Eugen. Rec. Office Bull.*, No. 22, xxxi.: No. 1, Psychological monographs.

STANTON, HAZEL M. 1923. An experimental investigation of musical inheritance. *Eugenics, Genetics, and the Family*, i. 239-242.

STEWARD, D. D. S. 1929. Notes on a pedigree of amaurotic family idiocy (Tay-Sachs disease). *Brit. Med. Journ.*, i. 101.

TIMME, W. 1924. The so-called unit characters in relation to hereditary disturbances of the nervous system. *Arch. Neurol. and Psych.*, xii. 131-136.

URQUHART, A. R. 1909. Insanity. *Treas. Human Inheritance*, pt. iii. 61-69, pls. 2.

VICARI, E. M. 1923. Hybridization and behaviour. *Eugenics, Genetics, and the Family*, ii. 75-77.

VOGT, C. and O. 1922. Pathoarchitectonik und Psychotische Erkrankungen. *Libro en Honor de D. S. Ramón y Cajal*, ii. 265-289.

WEISSENBERG, 1927. Erbliche Nervenkrankheiten. *Arch. f. Rass. u. Gesells.-Biol.*, xix. 425-426.

YERKES, R. M. 1913. The heredity of wildness and savageness in rats. *Journ. An. Behaviour*, iii. 286-296.

ZIERMER, M. 1908. Genealogische Studien über die Vererbung geistiger Eigenschaften, nachgewiesen an einen Material von 1334 Waldauer Haushaltungen. *Arch. f. Rassen. u. Gesells.-Biol.*, v. 178-220, 327-363.

CHAPTER XVI

RACIAL CROSSING

VERY important advances in our knowledge of racial crossing have taken place in the last five years, and they have resulted entirely from the application of analytical Mendelian methods to this subject. The methods of mass statistics and anthropometrical measurements have produced very little in the way of positive conclusions when applied to racial crossing. It is only by the study of individual pedigrees in racial crossing, as in the inheritance of single differences, that valuable advances can be made. All over the world families derived through two or three generations from crosses between different races are available for study; but they must be used to determine what characters show dominance in F_1 and how the numerous differences are redistributed in later generations. Mere mass statistics, unless collected and analysed with the greatest care, are worse than useless, and in any case cannot approach in analytical value the results to be obtained from the intensive study of even a few hybrid families.

This is emphasised because the time is rapidly passing when first crosses will be recent enough to obtain the whole resulting history. It is of prime importance that anthropologists should learn genetical methods of analysis and apply them in their field work to the human race. Every physical anthropologist should have a working knowledge of the methods and points of view of genetics and of the main results they have yielded in experimentation with plants and animals. The point of view is of the utmost importance in the analysis of racial differences. Very little of the work now being published by anthropologists is in a form in which it can be used in racial analysis. A great accession of trained workers in this field is highly desirable, but it is feared that without some genetical background very little of value will be accomplished. A newer genetical anthropology needs to be developed, but up to the present only a beginning has been made in this direction.

It is undoubtedly a fact that crossing between races has been taking place throughout human history and pre-history.

There is no such thing as a pure or homozygous race of mankind. When we examine the origin of any modern race, we find it compounded of two, three, or more elements, and in tracing them back in time we see some of their elements emerging from different races through isolation. Isolation has been the great factor, or at any rate an essential factor, in the differentiation of races;* while mingling and merging have clearly resulted in the production of many new races. Since man is a widely ranging animal, each of these processes has been tempered by the other, a period of isolation and stablising of a race often being followed by another in which parts of the race establish contacts which result in the absorption of fresh elements on a large scale from other races and the consequent production of a new "race."

Not only within the historical period (see, for example, Haddon, 1919, or Jochelson, 1928), but also among the races of Neolithic and Palæolithic man there is evidence of the frequent shifting of peoples in various parts of the world. Sometimes the defeated race was driven out or exterminated, but very often such migrations resulted in the fusion of two races into a new unit ultimately having certain uniform and distinctive features. The women of the conquered race were commonly taken as wives or slaves by the conquerors. It is evident that hybridisation has been going on in this way at intervals throughout the history of man. It does not follow, as some writers assume, that crossing is the cause of the evolution, but it does follow that the great majority at least of modern races are hybrid in origin, although they may have become quite uniform through isolation and inbreeding. The fact is that any racial unit contains the potentialities of innumerable minor races if these could be separated out and inbred. The range of migration of a people is an important element in determining how many distinct types will occupy a given area of territory. When the Indian tribes of the central plains of North America took to a nomadic life after the introduction of the horse, many of the tribal differences between them quickly disappeared. Differences can only grow up in a condition of isolation. This evolutionary principle of isolation

* This was emphasised by Sir Arthur Keith (1929) in his recent Huxley Lecture before the Royal Anthropological Institute, but he would apparently assign a minor value to crossing in the production of races. The present writer would also agree with this view as regards the production of the main varieties of mankind.

is of enormous importance and has usually been overlooked by anthropologists.

All human races therefore vary within wide limits because they are heterozygous for a multitude of factors. The conception of race can then only depend upon the selection of the commonest and most conspicuous and distinctive of these genetic factors, as giving the main facies to the race, and neglecting the less frequent and more inconspicuous ones. Thus we say that blue eyes and fair hair are characteristics of the Nordic race, although no modern community consists solely of individuals having these characters, and quite possibly no such commuuity ever existed. Similarly we say that a certain range of cephalic index is characteristic of each race, although it is becoming clear that these head shapes are the result of a number of interacting genetic factors, and that the individuals of any race will differ considerably in the particular combination of factors for head shape which they possess.

Certain generalisations from observations on racial crossing have been made by Hooton (1923), who is superintending anthropological studies of racial crossing in various parts of the world. In races with a high, narrow nasal bridge crossed with those having a low bridge (negroids, Mongoloids) the bridge is usually high. A broad nasal aperture is less affected by crosses, the F_1 being nearly platyrrhine. The complex cranial sutures of European skulls, in crosses with other races having simpler sutures usually show the complex sutures. Prognathism is regarded as a simian reminiscence seen in primitive races. In crosses between prognathous and orthognathous races the prognathism nearly or quite disappears. In crosses between negroes and whites the curvature of the hair decreases with decrease in the amount of negro blood, octaroon hair being usually dark, coarse, and quite wavy, but sometimes golden, fine, abundant, and wavy.

Tanning and freckling are regarded as phenomena of race mixture, arising in crosses of blonds with brunettes or pigmented races. A pure blond does not freckle or tan. In Hottentot-Boer hybrids some individuals tan darker than the dark race. The more primitive racial feature in crosses often appears to yield to the specialised, as in cranial sutures, thick lips, high nasal bridge, and prognathism. But there appear to be exceptions.

Hooton (1926) divides mankind into four main groups—whites, negroids, Mongoloids, and intermediates—each group

including at least three races. The intermediates are regarded as mostly the stabilised results of crossing between races, but it is recognised that the Australians and Ainus may be survivors of ancient generalised races. Keith (1929), on the other hand, believes that intermediate races are the incomplete results of evolutionary differentiation between races, and would apparently assign to crossing a very minor place in the origin of races.

The early work of Broca (1864) is of very much interest in connection with racial crossing, as it gives a picture of the hybrid conditions at that time in various parts of the world. He strongly emphasises the frequency of hybridity in mankind. As regards the French he says (p. 17), " I have been enabled to find in the present French nation, in the midst of the innumerable variations of stature, complexion, hair, eyes, cephalic shapes, etc., which may everywhere be expected in mixed races . . . the characters of these different races, and to recognise the more or less marked and dominant impress of the Celts, Kimris, Romans, and Germans." He believed that in different races of mankind there were various degrees of " eugenesic hybridity " or interfertility, and accounted for the supposed paucity of offspring from crosses between Australian or Tasmanian natives and Europeans by decreased fertility between distantly related races.

It may be worth while citing one or two from many instances where races have been altered by crossing or new races have been created in this manner. According to Haecker (1918) the Magyars lost their original characters when they came into Middle Europe from the East as riders about A.D. 800. They originally had broad faces with snub nose and yellowish skin. But since the tenth and thirteenth centuries they have rapidly mixed with European peoples and now only the language points to their former home between the Altai and the Urals. Similarly the modern Turks. Originally the pure-blooded Turk type, as now seen in the Kirghis, had a brachycephalic head, dark eyes with the Mongolian slit, a flat nose, small beard and yellowish skin. But these characters are seen in very few modern Turks, owing to mixture with Armenians, Arabs, Jews, Greeks, and south-western Slav women. Only the language again harks back to Central Asia.

In discussing the origin of the Jews, Salaman (1922) points out that despite their persistence as an entity since the disper-

sion, they are not a pure race, but were compounded of four chief strains, Arab, Amorite, Hittite, and Philistine. Sprung from an original Semitic Arab stock, the Habiru, they mixed freely with the other three stocks mentioned, the Hittites and Philistines being non-Semitic. In these mixtures the Hittite characters dominated the others, and as a result the majority of modern Jews present completely the Hittite or Armenoid type. The evidence from sculptures and other sources shows that in 3000 B.C. the Sumerians of Ur of the Chaldees had round heads, large aquiline noses, and short thick-set bodies, with clean-shaven skull and face. This is the Armenoid type which Salaman regards as related to the Hittites and probably to the Alpines of Southern Europe. The Hittites had large round heads, puffy faces, rounded nose and marked nostrility, as in the Jews. Early sculptures also show a people tall, with long heads and faces, long beards, nose not long or curved, but big and blunt-ended. These are Semites, very similar to Egyptian portraits of the Semitic Bedawin or Habiru. A third type so recorded were round headed with broad short face and small rounded features, small nose and high cheek bones. These were probably Kassites from Central Asia. All these races blended in the Babylonian Empire, and the sculptures of the period show mixtures of Semitic and Armenoid characters.

The arched nose and curved nostril of the Jews then came in from Armenoid mixture with the original pure Semite stock. The Amorites in the Lebanon valley were probably the source of the white skin, fair complexion, and red-haired blond type seen both in Jews and Samaritans. The Hittites were white with black hair and eyes and the aquiline "Jewish" nose. The Israelites who left Egypt about 1225 B.C. were an offshoot of an Arab-Hebrew race entering a land already occupied by the Hittites and Amorites. All these races intermingled as the Israelites gradually gained control of Palestine.

The Philistines, who were lost to history, must have fused completely with the Israelites. Salaman (1925) presents evidence for this view and regards them as belonging to the Minoan race from Crete. They had an athletic figure, small waist, long head, regular and delicate features, with nose and brow in continuous contour, hair and eyes black, skin white. The pseudo-Gentile type, which numbers about 20 per cent. of Jews, he regards as derived from the Philistines and not from modern Nordic mixture. The Hittite (Armenoid) type is dominant in this cross, as it is also dominant in modern Greece

over the classical Greek type which now occurs in but a small proportion of that people.

The original Hebrew would appear then to have amalgamated first with the Amorites, then with the Hittites, and later with the Philistines—all before the return from Babylon, 500 B.C., after which date the Jews were largely inbred.

The Samaritans also were originally complex in origin and considerable in numbers, but they have so dwindled that for the last two centuries they have never counted 200 souls. They have closely inbred for centuries, and now exist more as a family than a community. As a result, the majority of them show an amazing family likeness, but a minority is of different type. They are mostly dark-haired with sallow complexion, but some are blond, with very red hair and light coloured eyes.

The same mingling of races has been happening in modern times, on a small scale in many isolated parts of the world, and on a larger scale than ever before in such regions as South America. In Brazil, for example, there is not and never has been any "colour line," and for at least three centuries intermingling of Portuguese, Indians and negroes has been taking place freely. The present result is a population with every shade of skin colour from black to white, and in which every assortment of Indian, negro and white features and hair characters can be found. A pale coffee colour is regarded as the typical shade for a Brazilian. A few observations on this subject are recorded elsewhere (Gates, 1927). The offspring of a Portuguese man and an Indian woman have a swarthy, yellowish skin, very black eyes, and jet black, straight hair. Many cases of segregation and recombination of characters are seen in the population—*e.g.*, a man with entirely white features and dark skin, or one with white skin and brown kinky hair, or again one with white skin, light brown eyes, brown non-kinky hair, but thick lips and a broad flattened nose. On the other hand, some skin colour and half-kinky hair might be combined with thin lips.

It is open to doubt whether even such an isolated and primitive race as the Australians belong to a single pure stock. Davenport (1925) has made some observations on this matter. He points out that Topinard concluded that there were two races, of Malayan and Papuan origin: (1) Tall, dolichocephalic, with lighter skin and straight hair; (2) *more* dolichocephalic, short, with black skin and frizzy or curly hair. But the view has also been held that these differences have arisen

in Australia through germinal variation. Davenport expresses the view that the Australian natives are Neanderthaloids and not derived from the Dravidians. He made anthropometric measurements of six male and seven female full-bloods. They were extraordinarily dolichocephalic, with probably the longest legs of any race living, and skin colour darker than that of negroes in Jamaica or Bermuda. But there was great variability in skin colour, the hair being dark brown or black, usually wavy, but may be straight or curly, eyes dark brown. F_1 hybrids with whites had a skin colour like that of mulattoes, but with the yellow element not so high. Hence, even where a race has been isolated for ages, it is difficult to determine whether the variations it exhibits are of germinal origin or whether they result from crossing. It is clear in any case that there are now differentiated types on the Australian continent.

Segregation.

The important result which has been clearly proved in the last five years is that genetic segregation occurs in racial crosses just as in crosses between a normal individual and one having an abnormality such as albinism or hexadactyly. That segregation is not confined to abnormalities is shown by the fact that the blood groups, no one of which is any more "normal" than any other, are inherited as simple fixed Mendelian units (see Chapter IX). The only racial difference as regards the blood groups is in the frequency of the different types.

It may here be pointed out, however, that there is a general difference between, at any rate, many racial characters and single abnormalities; which is, that the former appear to be often represented by multiple factors while the latter are usually represented by single factors. This difference is of some importance. The opaque "black" eye and dark skin of a negro each appear to depend upon the presence of two or more cumulative factors in comparison with the blue eye and white skin of a Nordic. Similarly, the difference between extreme brachycephaly and extreme dolichocephaly must be determined by a number of genetic factors. It is doubtless the presence of these multiple factors in racial crosses which has prevented the general recognition of segregation in such crosses until now. A contributory condition has been the reliance upon mass statistics and the failure to collect and investigate individual pedigrees.

While the explanation of the polymeric condition of racial differences generally is not at present clear, yet it is possible that man with his 48 chromosomes is a tetraploid species, and that the double series of chromosomes in his gametes accounts for the double (or higher) representation of factors relating to so many characters. There are, however, certain difficulties with this view which we need not enter into here.

Certain racial characters appear to be of adaptive value to the race. Thus the narrow nose (high nasal index) of the Eskimos and some other races living under similar conditions prevents the intensely cold air from entering their lungs too freely. It seems clear that narrow nostrils would be a feature of survival value in such conditions. On the contrary, the broad flaring nostrils of the negro may have been of adaptive value in tropical conditions, though they may be merely a primitive feature retained, as in the Australians. Thomson (1913) first pointed out this relation between climatic isotherms and variations in the nasal index. From measurements of the nasal index of 2,681 natives of North and South America and 362 crania he found that noses are broadest near the heat equator and become gradually narrower towards Baffin Bay and Tierra del Fuego. It seems clear that the high nasal index (leptorrhine condition) of the Eskimo skull is a result of selection by the severe climate. On the other hand, the very broad flaring nostrils (platyrrhine nose) of negroes and Australian natives appears to be a primitive character retained. Thomson and Buxton (1923) in a fuller study conclude that the platyrrhine nose is associated with hot moist climates and the leptorrhine with a dry, cold climate, intermediates occurring in hot, dry, and cold, moist climates. They find a positive correlation between nasal index and temperature, also humidity; and that in the leptorrhine nose the respiratory passages are smaller and more split up. They find an extremely high correlation between nasal index and the index of the nasal aperture.

The relatively hairless body of the negro, as well as his skin gland specialisations and his intense pigmentation, may also be of adaptive value in the extreme conditions under which he lives. But such arguments will not apply to all racial differences or even probably to the majority of them. It is hopeless to explain hair characters from this point of view. Races probably have straight, wavy, curly, kinky or woolly hair because they have inherited it from an ancestor in whom

it first appeared as a mutation. The negro in Central Africa has woolly hair; the Indian on the Amazon, living in the same conditions, has straight hair which he doubtless derived from his Mongoloid ancestors.

The question has often been discussed, whether modern man is a single species or more than one, and opinions also differ as to the specific or generic rank of various races of fossil men. Hrdlička (1927), after bringing forward evidence in favour of the view that Neanderthal man was gradually transformed, by a series of steps, into modern man in the European area, feels it necessary to conclude that Neanderthal and modern man must therefore belong to the same species. But such a conclusion by no means follows. The fact that all the races of modern man are fertile with each other is no longer a sufficient reason for classifying them as one species.

The present generation of naturalists is describing innumerable species of plants and animals as distinct species, although they are perfectly fertile with each other. Sterility as a criterion of species has almost completely broken down. The origin, causes, and nature of interspecific sterility are still largely obscure, although polyploidy is known to be concerned in many cases in plants. But the conditions vary greatly from group to group. On the one hand, species of *Drosophila* so closely similar that they are scarcely distinguishable even by experts, may show complete sterility with each other, or at least produce only sterile hybrids. Self-sterility, which occurs in many plants, is known from recent researches to be a phenomenon of intra-specific sterility due to the presence and recombinations of certain genetic factors, yet certain of these combinations are required in order to produce the next generation. Thus sterility by no means goes hand in hand with specific differentiation.

On the other hand, all the species of cattle (Bovidæ) are interfertile, although many of them show striking differences, but in some crosses the interfertility appears to be incomplete. In this connection may be cited recent observations of Lus (1927) on crosses between the Yak (*Pœphagus grunniens*) and the Kirghizian breed of cattle (*Bos taurus*), the materials being collected during an expedition in Central Asia. As regards fertility, Kuhn's conclusion that the F_1 female hybrids are fully fertile when crossed back with either parent species, is confirmed. The male F_1 hybrids are at least partially fertile. In general, the F_1 hybrids are intermediate, but some show

more of the yak characters and some more of the cattle. Certain racial crosses in man appear similarly to give a variable F_1. But in later generations of the above crosses, segregation was observed in shagginess, length and bushiness of tail, character of the vertebral line, and position and curve of the horns, as well as in colour, form, and pigmentation of the muzzle and presence or absence of horns. Worth citing in this connection also are the results of Zavadovsky (1926), who has described crosses between the yak cow and the zebu bull in the zoological park at Moscow. The F_1 female was crossed back with the father and gave alternative inheritance clearly in pigmentation of hair, length of hair, and presence or absence of the zebu hump.

To return to mankind; there is then no necessity to regard all modern races as belonging to a single species, and the characters differentiating some human "races" are quite as great as those which are used in distinguishing many zoological species. The differences in the five great colour varieties of man are not only in skin colour but also in such points as stature, hair colour, and shape, cranial conformation, facial peculiarities, skin secretions, and intelligence. The differences between many species of higher animals are less varied and distinctive than these.

An anthropological survey of races is out of place here, but it may be pointed out that in the white population of Europe at least three races are now generally recognised: (1) Nordic, tall, blue-eyed and long-headed (dolichocephalic); (2) Alpine, short and stocky, brown-eyed and broad-headed (brachycephalic); (3) Mediterranean, small and slender, brown-eyed and long-headed. There is evidence that these have been intermingling in many areas throughout European history, so that the present result is a patchwork of many mixed types. Some anthropologists recognise other white races in the European area, such as the Dinaric or the East Baltic. Hildén (1927), who discusses the latter race, agrees with Retzius, Nordenstreng, and others in distinguishing them from the Nordics. He finds members of both the Nordic and the East Baltic race on the island of Runö (Hildén, 1925) in the Baltic, and concludes that they are found throughout Eastern Europe, including many parts of Russia, Finland, the Baltic States, and parts of Sweden. They are characterised in general by being blond (fair-haired with blue or grey eyes), brachycephalic, and with marked cheek-bones; but there are many other points in their charac-

terisation, and in Sweden they are different from the fair-haired brachycephalic type derived from segregation in crosses between Nordics and Alpines. It appears clear in any case that the Nordic and East Baltic "races" are more closely related than either of them is to the Alpine or Mediterranean. On the other hand, the gap between any of these races and the negro or Australian native is a conspicuously wider one. Although all Europeans belong to one "species," it does not follow that negro, Polynesian, and Australian races all belong to the same species. We may at least look upon the differences involved as of specific rather than varietal rank. We have seen that in Bovidæ intergeneric crosses show segregation of characters, so it is not surprising to find the same thing happening among the "races" of mankind.

The Endocrine Glands.

In seeking further for the genetic bases of racial differences, we soon realise that the phenotypic or visible external characters are not necessarily each directly controlled by a different genetic factor. Rather there appears to intervene between the germinal elements in the chromosomes and the "finished" characters a set of intermediary substances (hormones) secreted from the endocrine or ductless glands, each of these secretions affecting various parts of the body. We must assume that many racial differences are determined by differences either in the quantity or quality of these secretions, and that the latter differences are the inherited units determined by the genes. Probably the racial characters so controlled are chiefly matters of skin colour, stature, head form (in part), and various facial features. There is no indication that eye colour is concerned in any way with hormones, nor do hair characters appear to be under hormonic control, but the quantity and distribution of hair on the body is undoubtedly under such influence. How the genetic differences in the intelligence of races may be determined is unknown, but presumably they depend upon differences in the structure of the forebrain.

The endocrine glands, at least twelve of which are now recognised, are thus probably of great importance in racial analysis. They pour directly into the blood minute quantities of hormones which, acting as catalysts, influence and control directly the activities, and probably to some extent the development, of various organs. They also form a system of checks

and counterchecks to each other, and so constitute as it were an interlocking directorate, exercising the most complete control over the bodily activities as a whole through the medium of the substances which they discharge in minute traces into the blood. These glands have a very long evolutionary history, being derived in evolution from the transformation of totally different organs having other functions, and which are present in the lower vertebrates, such as Amphioxus, Petromyzon, and Tuatara.

In his presidential address to the Anthropological Section of the British Association, Sir Arthur Keith (1920) discussed the basis of differentiation of mankind into racial types, and showed how the characteristic racial differences are probably connected with differences in the secretions of the endocrine glands.* He pointed out that the characteristic differences of features, build, and colour cannot (for the most part) have been evolved directly by natural selection of variations, and elaborated the view that the differences observed are a result of variations which have arisen in the organs of internal secretion. These glands are now known to control in a marvellous manner the processes of development and functioning of the body. The principal of these organs are as follows: (1) The thyroid (a gland in the neck, astride the trachea); (2) the parathyroids (four small glands close to the thyroids); (3) the pituitary (a small reddish organ at the base of the skull), of which the anterior and posterior lobes have different functions; (4) the pineal body (a small gland, about the size of a pea, under the brain, resting on the anterior corpora quadrigemina); (5) the suprarenal capsules, over the kidneys, consisting of cortex and medulla, with different origins and diverse functions; (6) the islets of Langerhans in the pancreas; (7) the interstitial tissue of the reproductive glands (gonads). These glands pour directly into the blood which bathes them extremely minute quantities of their various secretions, and the latter control in remarkable fashion both the development and functioning, not only of the body, but also to some extent of the brain and mind.

The first instance in which the form of the body was found to be influenced by an internal secretion was that in which a pathological condition of the pituitary was shown to be the cause of the condition, known as acromegaly, in which there is enlargement of the bones and flesh of the hands, feet, and face.

* Keith has recently (1929) developed the same thesis further.

Enlargement of the pituitary is also frequently associated with gigantism. Dwarfism may result from an invasion of the pituitary by tumours, and also from a failure of functioning on the part of the thyroid. If such conditions are induced by deranged functioning of these glands, it is reasonable to suppose that corresponding racial (inherited) differences would arise from germinal changes, whose effect is to alter the quantity (or quality) of these secretions. The white race, according to Keith, shows a greater predominance of the pituitary than the Negro or Mongol, as indicated by the pronounced nasalisation of the face, the tendency to strong eyebrow ridges, prominent chin, and the tendency to greater stature and bulk of body. It is also suggested that the beardless face and almost hairless body of the representative negro and Mongol types is due to a lesser activity of the interstitial glands, the long stork-like legs of Nilotic and other tribes resulting from a greater abeyance of the same glands.

In the same way, differences in the pigmentation of the skin, which characterise the various races of mankind, may be reasonably assumed to be due to inherited differences in the activities of the suprarenal bodies, since it is known that Addison's disease, in which, among other symptoms, there is a darkening of the skin through deposit of pigment, is the result of a pathological condition of the adrenal cortex. Thus, the great colour varieties of mankind are probably determined in part by differences in the activity of the adrenal bodies; but it is probable that other glands as well are concerned in the determination of skin pigmentation, and we have already indicated some of the other racial differences which they probably control. If, then, in the various races hereditary differences in the activities of these glands of internal secretion are concerned, it may be expected that the results of racial crosses will be very different from what they would be if there were direct determiners for the various individual visible characters. For each endocrine gland has various activities and affects the development of many parts of the body. In crosses between races, whole complexes of characters would then be expected to be inherited or modified together. If the difference between a white and a black skin is due to the greater activity of the suprarenals in the white race, then it would appear that quantitative differences in the activities of these organs are the colour units really involved in white-black crosses.

The laws of quantitative inheritance are by no means fully understood at the present time, nor are even the facts of colour inheritance in mankind yet entirely agreed upon. Nevertheless, there are a number of cases of segregation of size factors in the recent genetic literature, and it is reasonable to suppose that quantitative factors of other kinds will also show segregation. But if the various skin colours are due to inherited differences in endocrine activity, we have here the basis for a further analysis and understanding of the combined phenomena of blending and segregation in the colour inheritance of racial crosses.

The thyroid is considered by Keith to be anthropologically the most important of all the endocrine glands. The thyroid, like all these glands, is believed to throw off two types of substances,* one which is morphogenetic and affects the development, the other which controls and regulates various activities of the body through the minute traces of certain substances which it pours into the blood. The latter substance in the case of thyroid is known as thyroxin. It has been isolated and its chemical structure determined, the molecule being found to contain iodine and arsenic. About 150 grains were obtained from some 6,000 pounds of ox thyroid, so that the amount of thyroxin poured daily into the blood of man must be almost too infinitesimal for computation. The condition known as myxœdema,† which is accompanied by peculiarities of the skin and hair, disappears when thyroid extract is administered. Berman (1921) cites the fact that, as early as 1891, sheep thyroid was administered to a woman with myxœdema. The symptoms disappeared, but she was obliged to continue taking thyroid extract until her death in 1919. In this period of twenty-eight years she consumed nine pints of thyroid, equivalent to the extract from the glands of 870 sheep.

Hence the thyroid acts directly on the skin and hair, which are the chief structures used in classification of the races of mankind. It also affects the skeleton, and when deficient,

* It may be questioned whether there are really two types of substances given off, one early in development and the other after maturity. It appears rather that a germinal change in, for example, thyroid production causes morphogenetic changes which will be inherited, while a functional derangement of the same kind occurring later will produce different results and not be inherited.

† A condition with dropsy-like swelling caused by failure of nutrition from defective nerve influence. It is associated with atrophy of the thyroid, and is probably directly due to excess of mucin in the system. It is accompanied by sluggish movements, thick speech, and dull mental condition.

causes, according to Keith, arrested development of the basal part of the skull, the root of the nose appearing to be flattened and drawn backwards between the eyes, the upper forehead projecting or bulging, the face being flattened, and the bony scaffolding of the nose greatly reduced. These are all characteristic features of the Mongolian face, and to a lesser degree of the negro face. Hence, it is concluded that a reduction or alteration in thyroid activity has been a factor in determining some of the characteristics of these races. The Mongol might be characterised as subthyroid relatively to the white man, while the negro is relatively subadrenal. Similarly such Eastern races as the Malays, Siamese, Chinese, and Japanese, having nearly hairless faces and little hair on their bodies, may be classed as in some respects eunuchoid, with a weak secretion from the adrenal cortex. They are, however, vigorous and prolific, and *these* are not eunuchoid characteristics. The social dominance of the white man might, then, be said to be due to the greater concentration of certain hormones in his blood.

Achondroplasia (see p. 42) is a form of dwarfing due to hypothyroidism, and is inherited. In man it may be accompanied by shortening of the face (prosopia), as in the bull-dog, or the face may be unaffected, as also in the dachshund. The latter condition is much less common. Short limbs and a long trunk, accompanied by retraction of the nasal region of the face, are all, according to Keith, Mongolian characteristics. The so-called Mongolian idiots (see p. 270) are stunted individuals, imbeciles with Mongoloid features. Their occurrence among Caucasian offspring is not an indication of Mongol ancestry outcropping, but is a form of hypothyroidism. On the other hand, enlargement of the thyroid causes goitre, and there are particular regions, as the vicinity of the Great Lakes of North America, where goitre is more frequent owing, apparently, to insufficiency of iodine in the water (see p. 224). According to Berman (1921), the thyroid also controls the speed of living. With more thyroid one thinks and acts more quickly. One milligram of thyroxin is found to inerease the rate of metabolism 2 per cent. Cretin babies fed on thyroid may undergo a remarkable mental and physical transformation to normal human beings, although the effects are often limited. But they must be fed on it all their lives, or they relapse into their former condition, because they are incapable of producing the secretion themselves. More recently Keith (1922) has elabor-

ated his views on this subject in an extremely interesting way, discussing such subjects as the Neanderthal skull, acromegaly, dwarfism, and many other anatomical alterations from the point of view of hormone control.

Seligman (1904) has described the frequent occurrence of "cretins" in Dexter-Kerry cattle. The breed appears to have originated, at Kerry at least, as early as the middle of the eighteenth century. One of its most striking features is the very short legs, which suggest a condition of hypothyroidism. In one herd fourteen cretins were produced among fifty-five calves in seven years. Another herd produced five cretins among twenty-seven calves in three years. These "bull-dog monsters" are non-viable, and abnormal in many respects. Their chief peculiarities are their short trunk and extremely dwarfed limbs (humerus only 13 millimetres in length), the extreme brachycephaly of the head with its rounded forehead bulging over the very depressed nose and upper jaw, while the lower jaw is normally developed. There is always a gap in the abdominal wall through which the internal organs protrude. The palate is cleft, the tongue long and protruding, while the thyroid is irregularly developed, and shows the same histological peculiarities as the thyroid of cretin children. It was probably devoid of proper secretion, as the extract of such glands produced little or no fall in blood pressure when injected intravenously.

This condition of cretinism was said to be constantly associated with placental disease, which would prevent the thyroid hormones of the mother from acting properly upon the young. But in at least one case a cow is known to have produced a normal calf following a cretinous one. Any defect in the placenta would then not be the result of a diseased condition of the cow, but rather the initial defect would be in the developing fœtus. Another fact which may be significant is the occurrence of 25·4 per cent. of "cretinous" offspring in the larger herd already referred to. This clearly suggests that the condition is a Mendelian recessive, due to a lethal mutation carried in the germ plasm of the breed, or in some of them. Further data would be required in order to verify this hypothesis.

Crew (1923) has made a study of the genetics of this condition, which bears out the above suggestion. He has also (1924) studied its pathology and ætiology. He cites the literature of human achondroplasia (1924), pointing out that it is not a

condition of arrested cartilage formation, but is due to arrest of bone formation in cartilage. Micromelia (short legs) and foreshortening of the face are mild forms of achondroplasia. The great majority of achondroplasic individuals are stillborn, but a few survive to become robust, muscular adults of small stature, with short limbs whose proximal segments especially are shortened. There are various other anatomical features, such as a large head with depressed bridge of the nose, and a thick wrinkled skin. The stillborn achondroplasic fœtus has various other, more extreme, malformations. Various inherited grades of the condition appear to exist, but it is not possible to form a race of typical achondroplasts, as was attempted by Catherine de Medici and others, because an achondroplasic woman cannot give birth to a child except by Cæsarean section.

The condition in the Dexter-Kerry cattle is of the most extreme type, the malformed stillborn calves showing brachycephaly, the bull-dog type of face and jaws, and extreme micromelia. This is recognised as achondroplasia rather than cretinism, and its immediate cause is ascribed by Crew to malfunctioning of the pituitary (which is smaller than normal) about the second or third month of gestation. It was shown experimentally that the pituitary from a " bull-dog " calf even at the sixth month contains very little of the hormone which expands the melanophores of a frog, although this hormone is active in normal cattle as early as the third month. The abnormalities of the thyroid found by Seligman are therefore regarded as secondary.

Crew agrees with Wilson that the short-legged Dexter-Kerry cattle probably resulted from a cross between the native black Irish Kerry cattle and the Red Devon, the frequent appearance of the malformed calves being due to recessive lethal factors. He supposes that the original Kerries had a factor B for black colour dominant to red, and the Devons a dominant factor S for short legs. The present Dexters are not only among the smallest cattle in Britain, but the definition of the standard of the breed shows that the most conspicuous points are brachycephaly and micromelia. When Dexters are mated together they produce four classes of calves—black and red Dexters (with massive head, stout body, and short limbs) and black and red Kerry (with slender head, slim body, and long limbs). The black Dexter is by far the most common and the red Kerry the least so, the other two types occurring in

nearly equal numbers, thus clearly suggesting a dihybrid or 9 : 3 : 3 : 1 ratio. The two pairs of factors would be (1) for red or black colour, (2) for the slim Kerry or stout Dexter bodily conformation. Since the old Kerry was black and slender, the other parent in the original cross must have been red and stout with short limbs—*i.e.*, Devons.

To account for the monstrous calves produced by the present breed, it is assumed that during the period of inbreeding following the original cross between Kerry and Devon, when off-type animals were being discarded in the attempt to produce a true-breeding black Dexter with short legs, two independent mutations, L_1 and L_2, occurred, which intensified the action of the factor for short legs (S), to which they are probably linked. Thus when the genetic combination SSL_1L_2 occurred, the resulting calf would be a non-viable monstrosity with excessively short legs and the bull-dog type of skull. Crew (1926) also describes a case of a Shropshire lamb twinned with a normal, born dead with the characteristic malformations of the bull-dog head but with normal legs. Several other lethal factors are known in cattle (see p. 30).

The niata cattle of Argentina, described by Darwin in his *Journal*, had a bull-dog head with prognathous lower jaw, upturned nostrils, and lips which failed to meet over the teeth. They apparently originated among the semi-wild cattle of the Indians of La Plata a century or more earlier, the Indians retaining them in preference to normal. When bred together they invariably bred true, and in crosses with normals the offspring were intermediate. It was also stated that the niata cow crossed with the common bull produced calves more like the niata than the reciprocal cross.

The extinct ungulate, Sivatherium, of India, a relative of the giraffes, apparently had a mild form of bull-dog face and jaw as a specific character. This condition also occurs in the carp and in the crocodile of the Ganges. I have observed what appears to be the same thing in a goose—*i.e.*, the upper bill shorter and turned upwards in a peculiar way. Some day we may hope to understand the causal nexus of events which begins with some germinal change causing endocrine derangements and ends with the production of these abnormalities.

Sir Arthur Keith applies the same conceptions of hormone determination to the anthropoid apes and other vertebrates, holding that in the orang there is a predominance of thyroid.

while in the gorilla the pituitary is predominant. However this may be, the view seems well-founded that racial differences in man, including the colour and character of the skin and hair, differences in physiognomy and in stature and the relative length of limbs, are related to inherited differences in the activities of various endocrine glands. This thesis will, no doubt, be further elaborated with inereasing knowledge.

The hormone view of human personality regards each individual, both in physical conformation and in mental activities, as a palimpsest of cross-patterns and developmental currents blended into a unified whole. Many elements of the personality must, however, be determined by mental differences based on inherited structural differences in the central nervous system.

Inheritance of Racial Characters.

The general facts of Mendelian inheritance in racial crosses from the anthropological point of view were recently set forth (Gates, 1926), but very important advances in our knowledge of this subject have taken place since then. Notwithstanding the many views which have been held as to what constitutes a race in man, and the numerous classifications of modern man—into three types, five or a score—there is general agreement that the most important racial characters relate to skin colour, hair colour and shape (causing straight, wavy, curly, or woolly hair), head form (including cephalic index), stature, eye colour, face, nose, and the eyelids (Mongolian fold).

The inheritance of stature has already been discussed (Chapter III.), as has that of eye colour (Chapter IV.). Here we may consider skin colour, hair characters, cephalic index as well as certain features of the face, nose, and eyes. It seems clear that the white race has arisen, probably through one or more mutations in skin colour, from a dark-skinned ancestral race. A definite race of albinos would undoubtedly have developed in Central America (see p. 114) in a similar manner had their own people not prevented intermarriage of albino individuals. Even with this inhibition (which is a eugenic act on the part of this primitive race, since these albinos have defective sight and other weaknesses) many individuals bearing this recessive character continue to appear in every generation.

Haecker (1918) attempted to draw a distinction between

two types of characters in racial crosses. Some characters, such as cephalic index and skin colour, are supposed to blend and gradually lose their marked character. These are of more complex origin. Others, such as eye colour and the Mongolian spot (see p. 317), segregate because they are formed by a simple or single process. It is doubtful whether any value can be attached to such a distinction. There is now evidence of two factors for the Mongolian spot, and different eye colours are now recognised as determined by a whole series of factors. We may next consider some of the general facts regarding the inheritance of racial characters.

Skin Colour and Hair Characters.

Skin colour, combined with hair characters, serves as the classical basis of distinction of human races. But it is obvious that the old classification into white, black, yellow, brown, and " red " races was not only inaccurate as regards characterisation, but also that it did not correspond with any genetic basis for the different skin colours. This is partly because the skin colour of each race is the resultant of the presence of black, yellow, and red (blood) pigments in different proportions; but also because the production and deposition of the skin pigments is apparently controlled by an intermediate mechanism of endocrine activity, which is in turn determined by the hereditary genes. When to this is added the fact that skin colour is very susceptible to the influence of exposure to the sun, it is not surprising that the unravelling of skin colour inheritance in racial crosses should be a difficult task still far from completion.

It does appear probable, however, that there is no difference in principle between the inheritance of brunette *vs.* blond complexion within the white races and the inheritance of the larger contrasts between white and the negro, Indian or Eskimo coloration, except that in the latter cases the difference is greater and, at least in the negro skin colour, multiple factors are involved. The fact that in a recent pedigree (Tomesku, 1928) a particular abnormality, clinodactyly (see p. 176), is linked with the brunette complexion and not found in blondes, is further evidence for regarding this difference in complexion as based upon a single pair of factors.

Hurst (1912) has summarised the studies on skin and hair colour in man, and added some observations of his own. The main points with regard to hair colour are: (1) That the brown

shades of colour appear to be continuous from white (albino) hair to jet black; (2) the reds form a separate series due to a lipochrome (a group of animal-fat pigments), while the brown is a melanin (a dark pigment found in hair, etc.); and (3) the generalisation of the Davenports (1909) that (with rare exceptions) children never have hair darker than their darker parent. This " non-transgressibility of the upper limit " applies also to skin colour or complexion in the white races.

Davenport (1913), from a study of mulatto families in Bermuda, Jamaica, and the United States, concluded that there are probably two segregating Mendelian factors for black, and that other negroid features, such as kinky hair and thick lips, segregate independently. The same would appear to be true also for mental characters, since mulattoes sometimes display high intellectual ability, but never pure negroes, as far as is known.

The evidence in favour of a strictly Mendelian explanation of colour inheritance in white-black crosses is, however, not yet conclusive. Pearson (1909), from data supplied by a medical man in the West Indies, gave quite a different picture. The first cross gives a brown mulatto or a yellow mulatto, and the basis or cause of this difference is not apparent. In crosses between mulattoes " there are now and then slight variations from the usual mulatto brown or mulatto yellow," but never pure black or white. Sports or throwbacks rarely occur, but the form where the tint is barely evident is said to be not uncommon. Mulatto × negro produces the sambo, a deep mahogany brown, and it is said there is never any other colour from this cross. Mulatto × white produces the quadroon, which is never pure white, but almost invariably lighter than the brown mulatto and nearly always lighter than the yellow mulatto. This gives the impression of intermediacy in the various hybrid conditions, with a not very marked tendency to segregation, which is never complete.

Evidently what is required in the first instance is an extensive collection of accurate data based on careful measurements of pigmentation with colour tops before the facts can be fully known. Probably something more complicated than the two-factor hypothesis of Davenport may be required to explain all the facts of colour inheritance in white-black crosses. In how far real permanent blends occur remains to be seen. Individuals certainly occur in later generations who pass for whites, and it is now also certain that the pigment is sometimes

entirely lost. Probably the presence of other negroid features often gives the impression that more black pigment has been retained than in the normal brunette skin. Cases of clear segregation in crosses of whites with negroes, Indians and Eksimos will be cited later (see p. 336). If the segregation is really between different degrees of activity of various endocrine glands affecting skin pigmentation, then it may be expected that the genetic results will be different from what they would be if skin colour was directly controlled by a few cumulative factors.

Jordan (1911), in a histological study of melanogenesis in mulatto and white skins, finds that the only factor in skin pigmentation is the number of (yellowish-brown) granules, and the number of cells containing such granules. Some mulattoes are identical with negroes and others with brunettes in amount of pigment. The apparent continuity in the melanogenetic process is believed to rest in mulatto families upon discontinuities or discrete units controlling the production of melanin granules. Such conditions conform more or less closely to an alternative mode of inheritance.

Sedgwick (1863) refers to silvery grey hair of very coarse texture as being present in about one in ten or twelve of the Mandan Indians, irrespective of age. This peculiar condition was more fully described by Catlin (1926).

The various types of hair in the different races of man—straight, wavy, kinky, and curly—are known to differ in the shape of a cross-section, straight hair being circular in cross-section, kinky hair elliptical, with the other types intermediate. Little is actually known regarding the inheritance of these differences. Bean (1908) has studied the hair types among the hybrid Filipinos, in which the Chinese element furnished the straight type of hair. Hair was classed as straight when the relative diameters in cross-section were 100 : 90 or over, wavy when 100 : 70-90, and curly when 100 : 60-70. In 31 families in which the cross was wavy × straight or curly × straight, there were 157 children, of whom 84 had straight hair to 73 curly or wavy. This approximates to a Mendelian 1 : 1 ratio; but dominance, when it occurs, is variable, and although segregation occurs to some extent, there is no close conformity to simple Mendelian behaviour. Wavy is regarded as a heterozygote of curly and straight, curly being recessive, but there is no sharp line between wavy and curly. Wavy × wavy gives all three types in approximately equal proportions. Straight

× straight gives all three types, but with a large preponderance of straight. Curly × straight gives mostly straight if the father's hair is straight, but more curly if the father's hair is curly. These results for Filipinos appear to be generally the reverse of those obtained in America. (See photographs in *Journal of Heredity* 7 : 412 [1916].) Bond (1912) cites certain cases of negro-white crosses in which wavy and kinky hair both appear in the same individual, the hair being wavy on the vertex and kinky on the sides of the head. Three such cases are figured.

Van Bemmelen (1928) has made an interesting study of inheritance of curly hair in his own family. He has traced this

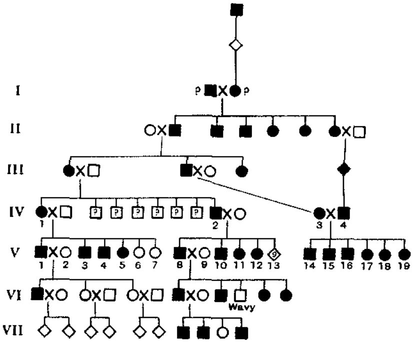


FIG. 72.—INHERITANCE OF CLOSELY CURLED HAIR. (After von Bemmelen.)

character in a parentela through several generations of his ancestors and relatives descended from a couple in the sixteenth century. The results are here thrown into pedigree form (Fig. 72), so far as this is possible from the statements given. It will be seen that the condition of closely curled hair has been traced through seven generations and appears to be inherited without exception as a single difference, although with some variability in dominance. Probably the original ancestors I. 1 and I. 2 both had curly hair since their six children all had it. In the fifth generation again, the parents (IV. 3 and IV. 4), who were related, both had curly hair and their

six children (V. 14-19) showed the same condition, but in varying degrees. In some of the children of the seventh generation the hair has just commenced to curl. A curly-haired boy may in certain cases become a straight-haired man. The reverse change may also take place, though less frequently. Such changes in the individual presumably indicate variable dominance, and the change may occur without apparent cause. In the racial crosses cited above, the same individual may have straight hair on one part of the head and kinky hair on another. It will be seen also that while curly hair is dominant to straigbt in the above pedigree, in Filipino crosses the Mongolian straight hair is more or less dominant to curly.

THE "MONGOLIAN" SPOT.

An extensive literature exists on the so-called Mongolian spot or sacral pigment spot, but only a few of the more important papers will be referred to here. The condition looks like a black-and-blue mark from a bruise, and is found in babes and young children of apparently all the pigmented races, including Koreans, Chinese, Japanese, negroes, Spaniards, Portuguese, Polynesians, American Indians, Eskimos and other races. Fig. 73 from Hansen (1893) shows the condition and some of its variations in Eskimo children. It is typically a faint bluish mark in the skin at the base of the spinal column. I examined it in two Eskimo babies of less than a year old in the Mission Hospital at Aklavik in the Mackenzie River delta. The nurse had noticed it and thought it looked like a bruise. An Eskimo girl of sixteen in the Hospital did not have it. In a recent paper by Suk (1928) he examined 53 pure-blooded Eskimo children from Northern Labrador. He found two kinds of spots: (1) dark blue and generally small; (2) very light blue and without distinct margin. They usually disappear at four years of age, but may persist to eleven years. He figures an extended series of the spots, in some cases partly covering the back, shoulders, arms and buttocks, with indications both of bilateral symmetry and of metameric repetition.

As early as 1885 Bälz made it evident that the presence of a blue fleck in the sacral region is a regular occurrence in young Japanese children. The pigment was found to be in the deep layer of the corium. Bälz regarded this spot as an important racial character, found only in Mongolians. Hansen (1893) next described this mark in Greenland Eskimo, regarding it

as a sign of relatively pure blood, and illustrating its variability. But a Danish missionary had observed it in Greenlanders over a century earlier. Adachi, in a histological paper in 1901, showed the presence of large pigment cells deep in the corium in the sacral region of white children as well as those of coloured races. But the cells are much more numerous in the latter, producing the dark fleck. Ashmead (1905) regarded it as a sign of negro descent in the Japanese—derived from the negritoid Eta of Japan. He states that it is not present in the Ainu,

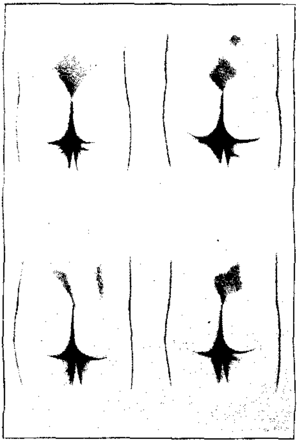


FIG. 73.—MONGOLIAN SPOT IN ESKIMOS. (After Hansen.)

but appears in crosses between Ainu and Japanese. It takes the form of violet spots on the buttocks, sacrum, or shoulders, which are commonly removed by ligature. They generally disappear in one or two years, but many remain throughout life. In Euro-Japanese crosses the spot is generally recognisable, but is wanting when the father had blond or red hair. It is usually paler and disappears earlier in crosses with whites than in the pure Japanese. Ashmead also states that the spot has been observed in the Indians of Vancouver Island and the

Mayas of Central America, but when the latter are crossed with Spaniards it does not appear. The Brazilians say that it is handed down in Indian crosses. In the Araucanian Indians of Argentina the spot is said to be not bluish but violet or maroon, nearly like the yellowish maroon of their bodies.

Fujisawa (1905) states that for 150 years Japanese doctors have tried to explain these marks, which are often near the shoulders or on the extremities, but very seldom persist to adulthood. In the clinic in Munich he found among 50 German children one with the spot. The parents as well as the child had dark hair and brown eyes. A second child from the same parents also had the mark in the form of three spots. There was no (known) Mongolian descent.

Brennemann (1907) made a study of the sacral spot in the American negro. Of 40 negro children under one year of age, 35 showed the mark distinctly, 4 were very light and 1 very dark in skin colour. He concludes that it probably occurs in over 95 per cent. of negro children, and gives many data regarding the occurrence of the spot in various races.

Some of the results of later study are given in a paper by Schohl (1913), who concludes that the mark is of general occurrence in the pigmented races, but also occurs more or less rarely in the white race. Both in white and coloured races the flecks are commoner in individuals of dark than of light pigmentation. He found no regular law of inheritance in crosses. The mark has been found in the fourth month embryo, it usually disappears in the fourth to seventh year, but may persist, especially when atypically located. The variability in form, size, and number of the flecks is emphasised, and the colour is found from the records to vary from light blue to nearly full black, seldom purple red, violet, or greenish. The surrounding skin is in every way normal, and the mark is not always easy to distinguish from nævi pigmentosi, vasculosi, and subcutanea hæmorrhagia. Pigment cells similar to those forming the fleck are found in many apes, either diffuse over the whole body or in certain places, giving a macroscopic pigment fleck. The significance of the fleck as a racial diagnostic character is regarded as doubtful. It is concluded that racial crossing is not the cause of the appearance of the fleck in the white race, but that it is atavistic in origin (Bloch's hypothesis) or a mutation (Apert's view).

Bahrawy (1922) made a study of the sacral skin of 112 cadavers, advanced embryos, newborn and young children.

He found pigment cells present in the corium in every case. They appear inthe fifth month of gestation and usually disappear in late childhood. The size of the fleck varies greatly, but may reach in newborn white babies nearly the size of the true "Mongolian" fleck. Hence the difference between white and coloured races is regarded as quantitative, in accordance with Adachi. A table of the geographical distribution of the spot is given, from which it is seen to occur in 1-2 per cent. of nurslings in Italy, 5 per cent. in Sicily, 2·4 per cent. in Sardinia, 1 per cent. in Paris, 2 per cent. in Budapest, 2 per cent. in Berlin. In Germany its frequency is estimated at 1 in 600, in Japan and Korea 90-100 per cent., China 97-98 per cent., Annam 80 per cent., Siam 89 per cent., Burmese 45 per cent., Hindoos 22 per cent. Java 99 per cent., Malaya 100 per cent.; also regularly in Sumatra, Borneo, Samoa, Hawaii, Philippines, and the negroes; very frequently in Tahiti, the Marshall Islands and New Zealand, Madagascar, Greenland and Alaska. In South America it is found in 87 per cent. of the Indians of La Paz, Bolivia. At São Paulo, Brazil, it occurs in 65 per cent. of the negro population, 52 per cent. of the mixed breeds, and 1·5 per cent of the whites.

Bruch (1924) regarded the pigment fleck in white children as a remnant of a wider ancestral pigmentation, or a spontaneous atavism. He thinks its frequent occurrence in combination with malformation is a sign that it may also be produced by injury to the germplasm, and regards as specially significant its combination with Mongolism in white children.

Two Swiss papers from the recent medical literature of the sacral spot may be cited here. Perrier (1925) points out that the presence of the spot in European children has often been considered as a last mark of the great invasions of the Asiatic hordes of Attila in the fifth century, Genghis Khan in the twelfth, and Tamerlane in the fourteenth. It appears to be extremely rare in Switzerland, and the author describes a single case seen at Fibourg during about fifteen years' practice with children. A female infant had a well-marked round spot, 1 cm. in diameter, over the sacrum. In colour it was slaty blue, a little darker in the centre. The child had brown hair and eyes; its mother was the same, a little Asiatic in type, while the father was also brunette. The author states as a known fact that the sacral spot never occurs in blond infants with blue eyes. Gautier (1925) estimates the frequency of the mark in European infants at from one in 1,000 to one in 200. It occurs

nearly always in very brunette infants from parents of the same type. It was seen in three infants: (1) A very brunette boy some months of age had two sacral spots. (2) A boy of Genevese parents, the darkest child of the family, with black hair and very brown eyes, had the mark at birth on the coccyx and on the lumbar region. It remained visible until he was four years of age, then became imperceptible except that in the summer when he was exposed to the sun it was visible at eight years of age. His sibs had lighter complexion and showed no spot. (3) A female child, three years old, showed one sacral and two dorsal spots. A physician who saw them reported the parents to the police for beating the child, which was very brunette with black eyes. The spots did not occur in its sibs.

Zarfl (1926), in practice in Germany, saw eleven children with blue birth-spots in five years. Ten of these were nurslings. Seven showed the characteristic condition, but three displayed a condition not previously seen in European children—*i.e.*, diffuse almost uniform blue colour of the skin on the buttocks. One also had flecks of pigment in the lumbar region; in another the whole back was covered with blue flecks to the shoulder blades; and in a four-year-old female child the blue colour appeared in the corium of nearly the whole trunk, especially on the ventral side. This was accompanied by malformations. The pigment pattern in this case resembles that in some apes and is regarded as indicating that the ancestors of man had a specific colour pattern in the skin. Sperck concluded that in the population of Vienna the Mongol fleck is only found in individuals having one or more Magyar ancestors.

A recent paper makes a thoroughgoing attempt to explain the inheritance of the sacral spot in racial crosses on a genetic basis. Larsen and Godfrey (1927) studied the spot in the various races in Hawaii, including Polynesians, negroes, Indians, Japanese, Chinese, Koreans, Spanish, Portuguese, and their crosses with whites. They quote the statement that in crosses between dark and white races the spot nearly always occurs, but is "fainter, less extensive, and disappears earlier," but they found that among 19 Portuguese it was large in 12, medium in 4, and small in 3. They also report it in 16 out of 150 "pure Aino."* They examined in all 693 children in Hawaii, including 296 from interracial crosses. Of

* *As the Ainus are known to have crossed much with the Japanese in the last generation or two, perhaps this is after all the source of their spot.*

75 Portuguese, 16 showed the mark, and 3 Spaniards out of 15 had it, hence about 20 per cent. in each case.

The following hypothesis was formulated to account for their results. P is a pigment factor, p its absence; o represents the mark (recessive) and O its absence. They assume that pigmented races are PPoo, the white race ppOo, and the Portuguese PpOo. Hence the mark will always be present in the dark races, while one factor for the mark is carried in the white race. The Portuguese are supposed to have one pigment factor, so that the mark will appear when oo is present. It is worth pointing out here that the Portuguese are known to have undergone much crossing with introduced negroes in the seventeenth century, and that this is probably why they are now heterozygous for one pigment factor.

The results from the various racial combinations are given in Table XIII. It will be seen that they are in excellent agreement with expectation based on the hypothesis.

TABLE XIII

	Total Number.	*Spot Present in.*	*Expectation.*
Coloured × Coloured	217	213	217
White × White	67	0	0
Portuguese × Portuguese ..	90	19	17
Coloured × White	68	34	34
Coloured × Portuguese ..	17	10	8·5
White × Portuguese	22	3	2·75

Head Form.

Certain facts bearing on the inheritance of cephalic index have been discussed at greater length elsewhere (Gates, 1925). Before taking up the question of the inheritance of head shape it will be necessary to consider it particularly as measured by cephalic index, in its relations to the body as a whole and also as regards its modifiability by environmental conditions. Reid and Mulligan (1925) concluded from measurements of 847 Scottish that the stature tends to vary inversely as the cephalic index (C.I.), stature appearing to be a determining factor in head length while head breadth depends rather on

the conformation of the skull. Fischer (1923) concluded that with increase in body length the growth in length of the skull is somewhat greater than growth in breadth, so that tall individuals will tend to be more dolichocephalic than short ones. This may be because a single factor (not the only one affecting stature) increases the length of skull and limb bones. Neubauer (1925) tried the experiment of growing rats on food devoid of vitamin A. He found that their skulls were not only smaller than normal, but much more brachycephalic, the C.I. ranging from 38·8-46·7, whereas in the control rats it was 34·9-38·0. Vitamin deficiency may therefore similarly affect the head shape in man, and in so far as differences in nutrition affect stature, so they may also have some effect on C.I. The better nourished classes of a population might thus tend to have a somewhat lower C.I. Fischer (1923) indeed states that the upper classes both in Europe and Japan have finer, smaller, and narrower heads than the lower classes.

Recently experiments of a mild kind have been made upon man himself. It is of course well known that various primitive races flatten their children's skulls by laying the babies against a board cradle, or otherwise deform them. Basler (1927) has recorded observations on the effects on skull shape of laying the baby, after birth, on its side or its back. Some evidence was obtained that habitually laying the baby on its back made the skull permanently more brachycephalic, while laying it on its side made the skull more dolichocephalic. The evidence can hardly be regarded as conclusive or entirely consistent, but certain of the more striking cases may be cited here.

Luise E., born in 1910 with C.I. 87·5, C.I. of mother 80·3. That of father is not given. The child was laid on its left side (afterwards on the right side), and the C.I. became gradually smaller, as the following records show: At one day old 87·5, three days 78·7, four days 79·1, six weeks 77·1, eleven weeks 76·8, sixteen weeks 73·8. When measured in 1925 as a girl of sixteen her C.I. was 77·67.

A pair of monozygotic twins were both laid on their back, Elsa on a soft cushion, Hedwig on a hard one, with the following results:

TABLE XIV

Age.	*Elsa C. I.*	*Hedwig C. I.*
1 day	83·5	87·15
18½ months	86·2	78·4
19 years	87·13	82·3

In another pair of monozygotic twins, one was laid on its side and the other on its baek, with the following results:

TABLE XV

Age.	*On Side.*	*On Back.*
1 day	88·39	85·08
3 days	87·50	86·48
8 ,,	86·72	87·71
16 ,,	85·12	88·35
31 ,,	84·80	86·05

In the years 1905-10, of 555 babies born at Stuttgart, half were laid on their back and half on their side. On the thirteenth day 84 per cent. of those laid on their back were more round-headed, and of those laid on their side 62·7 per cent. were more long-headed than at birth. A number gave evidence of having retained the determined form when seventeen to twenty years of age. Such facts as these obviously add to the difficulty of any study of head-shape inheritance. Similarly, it has long been known that the women of the island of Marken in the Zuider Zee, a primitive Nordic community, have their heads peculiarly elongated at the back. Since the men do not show this condition it was once suggested that this was a form of sexual dimorphism, but it turns out that the difference is directly due to their dress. Until the age of seven, boys and girls are dressed exactly alike, both wearing a cap which is tied tightly at the back of the head. This cap is then discarded by the boys, but the girls continue wearing it with a resulting deformation of the skull.

It has been generally recognised that women have rounder heads than men, and children than adults.

The conclusions of Boas (1912) require substantiation before they can be accepted. From an extensive statistical study of immigrants into the United States and their descendants he found that whereas the C.I. of Sicilians increased in America from about 78 to over 80, the C.I. of Eastern European Jews decreased from about 83 to 81. Of these apparently contradictory results, the latter alone might be explained by increased nutrition. Boas (1920) further found that Spaniards born in Porto Rico have rounder heads than their ancestors in Spain or the Canary Islands, the C.I.'s being respectively 79·7 and 82·8, but this is at least as likely to be the result of crosses with the brachycephalic Indians as a direct effect of climatic change. Fischer (1926) cites a paper by Guthe in which it was found

that Russian Jews in Boston when American-born were two units less brachycephalic than the foreign-born. These results therefore tend to cancel each other out.

Schreiner (1924) made a study of the inheritance of head form in Norwegian recruits and Lapp families, and she suggests, in accordance with Toldt, that head form may depend upon primary factors affecting the chondrocranium and secondary factors influencing the later growth of the skull, these hereditary factors being also very justly regarded simply as developmental tendencies.

Having referred to some of the numerous external and internal conditions which influence the cephalic index, we may point out that it has probably been much overrated by anthropologists as a racial character, and that very different skulls may have the same C.I. Haddon (1924) shows how in many races the C.I. has a wide range. That the same is true for quite small inbred populations is shown by the measurements of Ruhnau (1925) on the inhabitants of the little East Friesian island of Spiekeroog. They number 215 and are practically all intermarried, yet the C.I. for 63 women ranges from 73·3 to 92·4. Little or no meaning can be attached to the mean value, 80·45. Similarly Hildén (1925, 1926) measured the heads of the population (268) on the island of Runö, which are descended chiefly from Swedish (Nordic) men who married Esthonian (East Baltic) wives. He plotted the C.I. separately for both sexes and found that each gave a bimodal curve. Fischer (1923) states that the Boer-Hottentots of South-West Africa and Indian-white crosses in North America also give bimodal curves of C.I., thus indicating some form of segregation. Boas (1907) found something similar in the C.I. of Jewish families in America. A striking instance of such segregation is given by Kirkconnel (1925), who states that the C.I. of his father is 85, and that of his mother 72, while the children in order of age were 82, 85, 68, 73, and 83. Three were thus brachycephalic like the father and two hyperdolichocephalic like the mother. They all resembled in other respects the same parent whose C.I. they had inherited. The ancestors of this family had lived in the same locality in Ontario for over a century.

From a study of certain Malay hybrids, Hagen (1906) concluded that brachycephaly is dominant to dolichocephaly. Bryn (1920) studied the head form of families in two Norwegian districts and found segregation in the C.I. of the offspring.

He concluded that brachycephaly is dominant to dolichocephaly and mesocephaly. Bryn thinks that when brachycephaly is inherited from the father the sons are more pronouncedly brachycephalic than the daughters, but where brachycephaly is from the mother the daughters are more brachycephalic than the sons.

Frets, in a series of papers (1917-23) has attempted to analyse skull shape into a number of factors influencing the three dimensions and without dominance of individual factors. He treated statistically the results of head measurements made on 3,600 people belonging to 360 families, comparing parents with children. Later he concluded that brachycephaly was generally dominant to dolichocephaly, but in some families he found microbrachycephaly (small round heads) recessive to dolichocephaly. From families where the children show a greater range of C.I. than the parents, Frets concluded (1) that there is a large non-hereditary variability; (2) there is segregation; (3) high C.I. is dominant to low, with a large range of variation in the heterozygotes. He also states that heads with a high C.I. average somewhat smaller in dimensions than those with low C.I., and he finds that illnesses in early life affect the head form. This is to be expected, since it is known that illnesses arrest bone growth, and the shape of the skull alters during development. Frets assumes that about a dozen size-factors are concerned in the inheritance of head shape, but this is highly hypothetical, especially when so little is known of the genetics of shapes in plants and animals. Something has been done with the inheritance of shape in fruits, but our knowledge is as yet rather fragmentary.

The hypothesis of Frets postulates two factors A and B for brachycephaly dominant to dolichocephaly, and two factors C and D in small heads recessive to dolichocephaly. He further assumes that the A factor causes growth in breadth associated with a smaller increase in length and height of the skull. Similarly, B alters all three dimensions of the head, and C also alters the length and breadth as well as the height. He thinks that dominance may be influenced by sex, dolichocephaly being dominant in men and recessive in women. He finds that sons tend to have the head form of their fathers, and daughters that of their mothers.

Hildén's (1925) measurements of parents and children were not extensive enough for conclusive results. He found that individuals which were phenotypically alike in head shape

were not always genotypically alike, which would be in harmony with a theory of multiple factors. It may also be pointed out that some size-factors may produce a larger increment of size than others, and that others might alter the shape by influencing two dimensions in different degrees. But all such assumptions are hypothetical at present. Hildén states that he regrouped Frets's data and found it in general agreement with his own results. The present account is designed mainly to point out the difficulties encountered by any hypothesis until our experimental knowledge of size and shape inheritance is more extensive. On a simple multiple factor theory, with dolichocephaly recessive, two ultradolichocephals should produce children all with heads like their own, while two hyperbrachycephals, if heterozygous, would produce a range of skull shapes.

The two facts which stand out in the subject of skull-shape inheritance are (1) that round heads are usually dominant to long heads, and (2) that striking cases of segregation in head shape can occur within a single family as well as in some interracial crosses.

Facial Types.

Closely related to skull characters are facial types. Reference may here be made to a paper by Suk (1928), in which evidence is brought to show the occurrence of facial types belonging to one race in members of a distant race, and without the intervention of crossing. Suk states that in Bechuanaland, Pondoland, British and Portuguese East Africa, Somaliland, Eritræa, and Egypt aberrant facial types occur occasionally among pure negroes, these types of features being Japanese, Indian, Arabian, or even European in character. Considering man's proclivities for wandering and crossing, the only type of features which it would be surprising to find in Central Africa would be the Japanese. But Suk describes a Swazi girl of ten or eleven with very light, slightly yellowish, brown skin, oblique eye-slits and characteristic breadth of face, having quite the appearance of a Japanese girl but with negro hair. She was among typical Bantu girls. Last summer, however, I found a Japanese married to a Hare Indian woman, and with a family of small children, at Fort Good Hope by the Arctic Circle, on the Mackenzie River. One therefore feels the need of strong evidence before concluding in any case that

the phenomenon is not the result of a recent or an earlier cross in which a set of facial characters have remained strongly linked in inheritance.

Suk also cites a report of Sarasin, who found natives with strongly European features in the interior of Celebes, and a skull which he found in Moravia having definitely negroid and prognathous characters. He also reports finding in Northern Labrador pure Eskimos, some of whom had features strongly reminiscent of the Indians. These and similar cases reported by Hrdlička among Alaskan Eskimos seem clearly to indicate the outcropping of a linked complex of features derived through inheritance from an earlier cross. It may here be pointed out that certain Eskimos with distinctly negro features have been recorded by Hansen (1893) and others. But a negro nearly reached the North Pole with Peary, and a certain Hawaiian native is known to have left descendants among the Eskimos in the Mackenzie River delta. Gossage (1908) records an English family with " tightly curled, short, woolly hair of the negro type," while the facial features were not in the least negroid. This family had a tradition of a Mexican ancestor several generations back. The condition was inherited as a simple dominant with 18 cases in four generations.

Perhaps Suk's best case is the occurrence of Jewish faces among the Melanesians, and he also cites the occurrence of Jews with negro features but without skin pigmentation. He interprets all such cases as due, not to crossing, but to the reappearance of a limited number of facial types which originated in the early history of the human species. All such facts should be carefully investigated, to determine if the possibility of crossing, immediate or remote, is excluded. Even if due to crossing they would show a remarkable persistence of facial types and their failure to disintegrate. This would presumably mean linkage in the same chromosome, or else a single germinal difference affecting several facial characters.

The Effects of Racial Crossing.

We must now consider the general effects of racial crossing in different parts of the world. There appear to be cases in which hybrid vigour or increase of size results from intermarriage between races, but in other crosses there is no evidence of such an effect. This subject is one which requires much

further investigation. Crossing in mankind may be regarded as of three types: (1) Between individuals of the same race. Such individuals, as we have seen, usually differ from each other in many minor characters and are also themselves heterozygous for many factor differences. (2) Between different, but nearly related, races; *e.g.*, between the Nordic, Mediterranean and Alpine or East Baltic races, or between different African tribes, or Chinese and Japanese stocks. Such intercrossing goes on continually without causing comment or raising serious problems. (3) Between more distantly related races. Here we might again distinguish (*a*) crosses between two primitive or two advanced races from (*b*) crosses between an advanced and a primitive stock. It is only the last type which raises serious difficulties, and is probably undesirable from every point of view. Of course there is no sharp line between the most advanced and the most primitive races, but all intergrades occur. Nevertheless, the distinction I have drawn is certainly an important one.

In the newer countries, such as North and South America and parts of Africa, the cross-bred races which have sprung up through miscegenation between Europeans and more primitive peoples are at a disadvantage from every point of view. Besides the social failure of adjustment, physical disharmonies result, such as the fitting of large teeth into small jaws, or serious malocclusion of the upper and lower jaw; or, as Davenport (1917*b*) points out, large men with small internal organs or inadequate circulatory systems, or other disharmonies which tax the adjustability of the organism and may lead to early death. Segregation of characters thus results in a motley assortment of types, with some primitive and some advanced mental, moral, or physical qualities in place of the original more or less blended condition in the first generation of the cross. It is questionable even if marriages between North and South European races are always wholly desirable in their results; although history shows, on the other hand, that the intermixture of more closely related races is beneficial as supplying increased vigour and a greater range of alternative characters, to increase the potentialities of the population or for selection to play upon.

In mankind the differences between the five great colour varieties are not merely in the skin colour, but also in such points as stature, hair colour and shape, cranial conformation, facial peculiarities, skin secretions, and intelligence. These

differences are quite as distinctive and varied as those between many described species of higher animals. Such differences could only have grown up during long periods of isolation, and can only be maintained by isolation or an absence of crossing. The five colour types of mankind also occupied, until modern transportation began, more or less markedly separated areas of the earth's surface, although where the yellow and brown races, for example, are in contact in south-eastern Asia a gradual transition occurs between them, which Sir Arthur Keith ascribes to evolutionary differentiation.

Where evolution has been going on independently in these races for such long periods, and some races have progressed far beyond others, both mentally and culturally, it is folly to suppose that crosses between a progressive and a primitive race can lead to a desirable result from the point of view of the advanced race, or even of the primitive race. Many native African and other tribes have scarcely emerged from the Neolithic period, so far as their culture is concerned, and it cannot be expected that their mentality has advanced beyond that period. The mental status of the average Palæolithic man is difficult to determine. Although the mental capacity of modern man has not increased during the historical period, yet it is necessary to suppose that the development of the human mind has consisted in something more than the mere accumulation of tradition. In other words, there has been a real evolution in which the mind has been one of the reacting elements. The mental level of the *average* Palæolithic man can hardly have been higher than that of our modern feeble-minded. The Australian black-fellow appears to be an early Palæolithic survival, resembling Mousterian man, and wholly incapable of coping with the white man's civilisation. It is clear that other races represent different stages of mental development.

This, of course, is often disputed, and it is frequently held that Palæolithic man was potentially the mental equal of modern civilised man. This depends on the sense in which the term "potential" is used. The important point is that primitive races are largely incapable of taking hold of the white man's civilisation and profiting by it, or adapting it to their own use, except in a primitive way. No doubt, as Carr-Saunders (1922) holds, man's mental evolution has consisted largely in the handing down of accumulated tradition, but there must also have been a reaction of man's mind—that is,

a mental evolution—in order to make the continued accumulation and advance of tradition possible. That such a mental evolution has accompanied the accumulation of tradition is evident from the recent history of the Japanese. They were able in one generation to absorb a great part of Western science and begin making independent contributions to that science. This remarkable phenomenon, resulting from contact with Western civilisation, has not been approached by any truly primitive people, which shows that primitive peoples would require a long period of mental evolution before they were capable of grasping or profiting by the views of nature held in the civilised world.

As we have already pointed out, crossing between more or less related races or tribes of mankind has been going on at intervals throughout the whole of historical and prehistoric time. Nevertheless, at any given period it has usually been confined to definite areas of contact between tribes, and has been very limited in its scope, except at times of migrating or shifting populations. Primitive man, in particular, was far less of a roving animal than is commonly supposed. This is shown by the great number of local native tribes which existed among the Indians of North and South America at the time of their first contact with European civilisation. Such differentiation, like that of any other species, could only have occurred under conditions of relative isolation and segregation—*i.e.*, absence or infrequency of inter-marriage. Carr-Saunders (1922) has pointed out that as soon as early man began to have any social organisation at all, probably even as early as the Upper Palæolithic, families and groups began to develop hunting and fishing and general food-getting rights over fixed limited areas. Among the primitive races of modern times these conditions continue. For instance, in parts of former German South-West Africa, where the chief Hottentot food-plant on parts of the coast is a gourd, *Acanthosicyos horrida*, growing on the sand-dunes, individual families and groups have vested rights over the fruits of this plant in local areas, and it annually saves their lives and serves as a source of both food and water until other food is obtainable.

Native groups are, then, not free to wander at will wherever fancy dictates, but each party is confined to a limited area, whose boundaries are definitely known to them. This fact, that each group is definitely tied to a local area by recognised custom and is often at war with its neighbours, adds greatly

to the stability of any savage population, and probably lessens the amount of exogamy between unrelated families. These are the conditions under which local tribes and differentiated groups might be expected to grow up. Such a process of differentiation is, however, very slow, and the spread of culture from group to group will also tend to the maintenance of uniformity. Nevertheless, cultural differences, owing to local environmental conditions, will arise long before structural differences appear, and in the tribes of North American Indians such structural differences seem to have been very few. Languages, on the other hand, were many and often widely different (though showing evidences of a common origin), which implied a long period of cultural isolation. A valuable study could be made of the relative rate of differentiation of a group of tribes, such as those in the Mackenzie River basin, as regards physical and mental characteristics and language. It is clear that lingual precedes physical differentiation.

The results of crosses between such related tribes are relatively insignificant, the differences involved being less than those between the peoples of European nations. Crosses between equally primitive or equally advanced peoples of similar culture involve no very serious problem. Inter-crossing between races more remotely related, especially when one is primitive and the other advanced, immediately involves problems of the utmost difficulty—problems which may be said to have arisen seriously only in modern times, although such crossing also took place in connection with some of the earlier civilisations. These problems require study in three separate aspects: (1) In crosses between primitive races; (2) in crosses between a primitive and an advanced race; (3) in crosses between advanced races. In each case the results of the particular cross must be taken into account. For instance, crosses between Europeans and Bantu peoples might be undesirable from any point of view, while marriages between Europeans and Polynesians might conceivably produce a more felicitous result.

. Wallace (*Malay Archipelago*, p. 335) states that "everywhere in the East where the Portuguese have mixed with the native races they have become darker in colour than either of the parent stocks"; but that "the reverse is the case in South America, where the mixture of the Portuguese or Brazilian with the Indian produces the 'Mameluco,' who is not unfrequently lighter than either parent, and always lighter than

the Indian." Such results might be expected if skin colour were controlled by differences in the activity of various endocrine glands.

The most ambitious of the earlier studies of racial crossing is probably that of Fischer (1913) on the Reheboth hybrid people inhabiting a portion of South-West Africa. These people were derived from crosses between Hottentot women and Boer men, which began over a century ago. They now number, perhaps, 3,000. In a general anthropological and ethnographical study of these people, Fischer concludes that they are a well characterised but very variable group. The characters of the parent races are combined in the greatest variety of ways, showing continued segregation, and not a permanent blend. The first crosses are, in general, intermediate, and when crossed back with either race, they resemble more the race with which they were recrossed. They are said to be sound, strong, and very fertile, having an average of 7·4 children per family. The inheritance of individual characters, such as hair form and colour, eye colour, skin colour, shape of nose, nasal index, form of eyelid, breadth of forehead, etc., was studied and found to show alternative inheritance; but the observations, while valuable, are scarcely sufficiently detailed to furnish critical evidence on all these points. Nevertheless, a body of valuable data of inheritance is brought together. An important conclusion reached is that the size of body and length of face is greater than in either parent race, while the fertility is found to be undiminished and the sex ratio unaltered.

The latter conclusion is, however, not in harmony with the statistical data on the sex ratio in hybrids obtained by other investigations. Thus, Pearl and Pearl (1908) examined the vital statistics of the city of Buenos Ayres, where Italian, Spanish, and Argentine crosses take place, the last being itself a mixed race. The data extended over a period of ten years, and made possible the comparison of the sex ratio in pure matings with that in crosses. In the former case the ratio was 102·21 : 100, in the latter 105.99 : 100, hence a greater excess of male offspring from cross-matings. Little (1919) has made a similar study of the sex ratios from the records of a lying-in hospital in New York. These records, unlike the previous ones, included still-births, and the types of matings included (1) those within each of the following nationalities: English, Irish, Scotch, Italian, Russian, Greek, Austrian, and German; (2) all possible first generation matings between members of these nationalities.

The results gave a sex ratio of 106·27 for the pure stocks and 121·56 for the crosses. This indicates an even more marked increase of male births in the hybrid stocks than the Argentine statistics. Separate examination of the data for still-births indicated that they were more frequent in the pure races than in the crosses. These results indicate that in crosses between European races there is a higher ratio of male births and a lower frequency of still-births, at least in the first generation. The latter is probably a result of hybrid vigour. That crossing a species may alter the sex ratio of the offspring in very marked degree has also been shown in the case of pigeons and other animals.

Returning to the subject of racial crossing, reference may be made to a short study of racial mixture in Hawaii (MacCaughey, 1919). In these islands intermarriages of Portuguese, Spanish, Hawaiian, Chinese, Japanese, Americans, English, and other Europeans are taking place. The population containing this remarkable diversity of races numbers about 246,500, the Japanese predominating in numbers. From a decade of observation of this microcosmic melting-pot, the conclusion is reached that such racial intermingling is usually undesirable in its results. Most of the Hawaiian-white hybrids seem to combine the least desirable traits of both parents, and intermarriages of North European and American stocks with dark-skinned races are considered biologically wasteful.

Similarly Lundborg (1920), from a study of Swedish conditions, concludes that the crossing of races degenerates the constitution and increases degradation. He finds such crossing much more common in the poorer and lower classes, while the middle classes are more homogeneous. In the lower classes are more frequently found individuals with other race characters—*e.g.*, darker hair and eyes. Mjöen (1922) has examined the results of crosses in Norway between the Nordics and the Mongoloid Laplanders. He found the first generation to be taller and heavier than the tall Nordic parent (owing to heterosis), but that this increase in size is lost in later generations. Also, frequently in crosses between Lapps and Norwegians, especially when Alpine blood was also present, a mentally unstable type is produced, the lack of balance being shown by stealing, lying, and drinking. A similar unbalanced type frequently arises from crosses between American Indians and French or English. The writer concludes that as regards these matings, the pure races have the advantage in every way.

For example, the incidence of tuberculosis is the lowest (1·1 to 1·5) where the Nordic race is comparatively pure, and highest (3·6 to 4) in the region where there is the largest race mixture.

As regards world eugenics, then, it would appear that intermixture of unrelated races is from every point of view undesirable, at least as regards race combinations involving one primitive and one advanced race. It is possible that crosses between an advanced and a native race may be advantageous as leading to progress in certain tropical regions where the white man cannot survive, although the results of such interbreeding in various tropical countries do not lead to a very hopeful outlook. But the melting-pot conception is being discredited by eugenic writers in the United States, where intercrossing has been taking place on a great scale. It may now be recognised that while interbreeding of related races or strains may give increased vigour, at least in the F_1 generation, crosses on a large scale between more distant races which have for ages been separately evolving create unnecessary problems, and are, for the most part, wholly undesirable in their results. The more advanced race is diluted and degraded by such intermixture, and primitive mental and moral characters are placed on a level with the more highly evolved. Moreover, Goddard (1917), in discussing mental tests for immigrants into the United States, states that the average steerage passenger is of low-grade intelligence, perhaps even feeble-minded. He examined six small groups arriving at Ellis Island, by means of the Binet scale tests, and found that only 2 in 148 scored as high as twelve years, which is regarded as the line between feeble-minded and normal. These people included Italians, Russians, Jews, and Hungarians. His conclusion is that there is a high percentage of feeble-minded among the present immigrants. It must be remembered, however, that a trans-Atlantic voyage under steerage conditions is not a very good preparation for such a test.

Even after a thousand years of intermarriage, separate racial traits may still be traceable in the modern Englishman. The blend is only a blend when considered *en masse*. Alternative inheritance, and more or less complete segregation, still appear as regards single characters. The various types of modern Italian, viewed in the light of their history, appear to show the same thing. Although innumerable racial unions have taken place in the history of mankind, yet the elements distinguishing the original races appear to retain their separate

identity and independent transmission in inheritance. The resulting race considered as a population will be a blend of the original races, yet, for a long period at least, the elemental differences continue to be separately inherited. Whether, ultimately, a real blend occurs is uncertain, but if it ever does this may be only after a thousand years or so of interbreeding within the hybrid race. In any case the racial elements of the more primitive stock will dilute and weaken the better elements of the more progressive stock, with a retarding or degrading effect on the progressive stock as a whole. It is, therefore, clear that miscegenation between, for example, the white races and African races—which for ages have been undergoing separate evolution which must have been at very different rates, assuming that both are descendants from the same original stock—is wholly undesirable from a eugenic or any other reasonable point of view.

Recent Results of Inter-Racial Crossing.

We may now consider some of the later results of crosses between different races. These observations are, for the most part, very recent, and some of those cited have not previously been published. In this work abundant evidence of segregation appears, and the whole subject takes on more definite aspects.

The question whether segregation occurs in racial crosses has long been disputed, and only now can it be quite definitely answered in the affirmative. Numerous clear cases of it will be referred to in the following pages. We may first cite a striking instance in a cross between Eskimos and whites. An Eskimo woman from Alaska married a Dane and had several children. One of the daughters, who would be half-Eskimo, married a Norwegian. She is shown in Fig. 74 with two of her three daughters. This photograph was taken on Great Slave Lake in 1928 and a full account of these and other mixed breeds will be published elsewhere. The half-Eskimo mother in Fig. 74 has intermediate skin colour, dark brown eyes, hair nearly pure black, fine and slightly wavy. Eskimos have fairly dark skin, very dark eyes, and straight black hair. The daughter on the right (Ida) in the figure has pure white skin without a trace of colour, her eyes are hazel, her hair almost flaxen, and very wavy, in fact quite the Nordic type of her father. The daughter on the left (Bessie) had only a trifle less skin colour than her mother, dark brown eyes, hair rather

light brown and slightly wavy. The older sister (Martina), who was not seen, was said to be not quite white, with eyes light brown and hair medium brown and wavy.

Hence in this back-cross of the F_1 to white we have three daughters, all one-quarter Eskimo, one of them with the white skin and Nordic hair and eyes of her father; another very similar to the mother; and a third intermediate. There is no absolute certainty that the Eskimo grandmother was pure-blooded, as there has been much crossing with whites in Alaska,

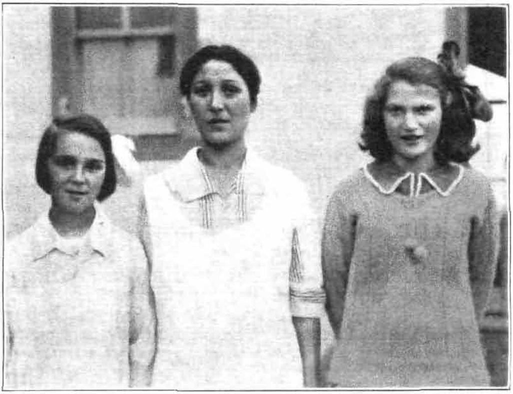


FIG. 74.—HALF-ESKIMO MOTHER AND TWO QUARTER-ESKIMO DAUGHTERS, SHOWING SEGREGATION.

but her features show no indication of hybrid mixture. If she is pure, and the back-cross gave segregation only between the white type of Ida and the half-colour of Bessie and the mother, then we should assume a single set of linked factors for these differences in skin, hair, and eye colour. But Martina appears to have been definitely intermediate, and so it may be necessary to postulate, not a set of linked monohybrid factors, but perhaps one or more endocrine differences which are also capable of being fractionated.

This baffling combination of sharp segregation in certain

individuals and dilution of the pigmentation characters in others appears to be characteristic of human crosses. It is difficult to believe that single-factor differences for skin colour and eye colour distinguish the pure Eskimos (although they are usually as light or lighter than mulattoes) from the blue-eyed Nordic; on the other hand, it seems unlikely that if duplicate factors are present a pure Nordic type would segregate in a back-cross generation of only three individuals. Nevertheless it appears likely that duplicate factors for skin, eye, and hair colour are involved between Nordics and Eskimos. This remarkably interesting case therefore calls for more evidence from other sources.

That only a trace of skin colour may appear in some of the descendants from a racial cross is frequently stated; and one of numerous instances which proves the truth of this statement may be cited here. When travelling in the Canadian North-West in 1928, the following observations were made. A waitress on the boat on Lake Athabaska was a brunette who stated that she was of pure white ancestry. She had no difficulty in passing as such; but the skin at the back of the neck and on the arms showed a sufficient tinge of colour to lead one to suspect that she might have Indian ancestry. Enquiry elicited the fact that on her father's side she was descended from one of the Lord Selkirk settlers in Manitoba, who took an Indian wife about 1820. Her mother, who was also on the boat, showed signs of Indian ancestry in her features, although she too was practically white. The girl, both of whose parents thus had a small amount of Indian blood, had very dark eyes, black wavy hair, perfectly "white" pretty features, and a dark creamy complexion with pink cheeks. The only indication of Indian ancestry was the slightly hyperbrunette skin colour on the areas mentioned.

Here is evidence, not only that skin colour can segregate from other racial characters, but that this colour character is fractionated so far as the phenotypic appearance is concerned. Since, as we have seen, skin colour appears to be controlled by the activity of various endocrine glands, the inherited units are presumably differences in the activity of these glands, and in these circumstances an apparent fractionation of skin colour could be produced when the inherited units controlling skin colour were not fractionated at all. This is the interpretation to be placed upon such cases until the evidence is more complete.

Other cases were observed in the Canadian North-West, in which individuals with an Indian ancestor had entirely white skin. A woman, whose maternal grandmother was one-quarter Indian (*i.e.*, one of her great-great-grandparents was an Indian and she would have one-sixteenth Indian ancestry), had clear white skin, light hair, blue eyes, and no trace of Indian features. She was the youngest in a family of nine, and some of her sisters had darker complexion with some skin colour. One whom I examined had nearly black hair which was nearly straight, eyes light brown and slightly Indian features, thus contrasting strongly with her fair sister. Segregation can thus be complete, leaving no trace.

We may next consider a few of the results of crosses between whites and Ojibway and Cree Indians in Northern Ontario, a full account of which has recently been published (Gates, 1929). So many cross-matings and intermarriages of related mixed-bloods have taken place in this area and the original interracial crosses occurred so many generations back that the results are difficult to disentangle. Several intermarried families show every degree of mixture of white and Indian blood.

The conclusions tentatively arrived at may first be stated. They are—(1) that two or more factors controlling skin colour are present in the Ontario Indians; (2) that one of these affects both eye colour and skin colour, or at any rate is closely linked with a factor for dark-eye colour, while another is not. A very dark skin is accompanied by intensely black eyes, but an intermediate skin colour may be combined with blue eyes having only a little yellow pigment. This indicates (3) the independent segregation of certain factors for eye colour and certain factors for skin colour. (4) The intensely "black" eye of the American Indian probably represents at least two factors for pigmentation. As regards skin pigmentation factors, the Indian may therefore resemble the negro, to be discussed later. It is possible that full-blood negroes have another factor for skin colour, since they are distinctly darker than Indians and Eskimos.

There is definite evidence that certain extinct Indian tribes in the Western States, the Mandans and Minnetarees, as well as some of the Crows, were nearly, but not quite, white (see Catlin, 1926). They had hazel, grey, and blue eyes, and their hair was of various colours but not red or auburn. This cannot be accounted for by crossing with whites, and must

have resulted from mutations in skin and eye colour similar to those which produced the white races of Europe. The Mandans also showed an extraordinary type of hair variation referred to elsewhere (p. 315). Sullivan (1920) reports finding among 539 Sioux Indian males supposed to be of pure blood, four with grey and five with blue eyes. However these Indians came by their blue eyes, their existence shows that eye colour has segregated independently of the hair colour, hair form, and facial width of pure Sioux Indians.

That variations probably independent of crossing can also occur in other races is shown by the following quotation from Père Lafitau* on the Eskimos of Labrador (cited from Jenness, 1921). He says: "They are tall, well built, and whiter than other savages. They allow their beards to grow, and have curly hair which they cut below the ears. Their hair is almost always black, but a few have light-coloured hair (Fr. blondes) and some have red hair (Fr. roux), like the people of North Europe." Another case is cited among the isolated Eskimos of the east coast of Greenland, where among 136 people one girl of twenty had blue eyes (*Med. om Grønl.*, xxxix. 177).

For details of the above-mentioned Indian crosses in Ontario, reference must be made to the original paper, but certain points may be illustrated here. Fig. 75 represents an Ojibway Indian family. Fig. 76 has about eleven thirty-secondths Indian blood (using the Galtonian notation). She had swarthy skin and black eyes. Fig 77 represents two sisters in a family of five. Their parents were both segregates having some Indian blood, the mother with hazel eyes and almost a white skin, while the father had bluish-grey eyes and almost white skin. Patricia (left) had brown eyes shading to yellow and grey at the margin, nearly white skin, and somewhat Indian features. Martha (right) had similar eyes, a pure white skin, and "white" features. Another sister, carefully examined, had blue-grey eyes with flecks of brown around the pupils, and a white skin. A fourth (younger) sister had eyes changing from blue to darker blue-grey, and white skin. The baby had brown eyes and white skin. The hair of all these sisters was medium brown except Patricia, whose hair was very dark brown. Thus where both parents had a small amount of skin pigmentation some of the children were devoid of this feature.

* Lafitau, J. F., 1724. *Mœurs des Sauvages Ameriquains*, vol. i., p. 55.

FIG. 75.*—AN OJIBWAY INDIAN FAMILY FROM TEMAGAMI, ONTARIO.

FIG. 76.—AN INDIAN-WHITE MIXED BREED, ABOUT $\frac{11}{32}$-INDIAN BLOOD.

* Figs. 75-79 are from *Journ. Roy. Anthrop. Inst.*, vol. 58.

FIG. 77.—INDIAN-WHITE SEGREGATION. LEFT, BROWNISH EYES, NEARLY WHITE SKIN, SOME INDIAN FEATURES. RIGHT, SIMILAR EYES, PURE WHITE SKIN AND WHITE FEATURES.

FIG. 78.—THREE BROTHERS ABOUT $\frac{3}{16}$-INDIAN BLOOD. SKIN COLOUR INTERMEDIATE, EYES NEARLY BLUE.

Fig. 78 shows three brothers of a family of fourteen, whose father was one-quarter Indian, and mother about one-eighth Indian, with medium skin colour and "blue eyes." These sons would then be about three-sixteenths Indian. They agreed in having considerable skin pigmentation, but blue eyes with only spots of yellow pigment around the pupil. Three other brothers were very similar in eye and skin colour, as were four sisters, but three other sisters had white skin. Finally, in Fig. 79 may be compared, from left to right, one-eighth Indian, one-quarter Indian, and pure white.

FIG. 79.—LEFT TO RIGHT, (1) ABOUT $\frac{1}{8}$-INDIAN, (2) ABOUT $\frac{1}{4}$-INDIAN, (3) SCOTCH.

One conclusion to be drawn from these results is that the inheritance of eye colour follows exactly the same laws in interracial matings as in marriages within the white race.

From carefully analysed measurements of several hundred Sioux Indians of pure and mixed blood, Sullivan (1920) has shown that in those of mixed descent the curve of variation for facial width is bimodal or two-peaked, an intermediate type of face rarely occurring. This is excellent evidence of dominance and segregation as regards the broad face of the Indian and the narrow faces of the white races with which they crossed. Head widths also fell into a bimodal curve, the values being highly correlated with those of face width. In those measurements in which Indians and whites differ most widely, the mixed

breeds showed lower correlation, again indicating independent segregation of characters.

A condensed but fairly full account of racial crossing in the Bonin Islands has recently been published by Goldschmidt (1927). These small volcanic islets are situated about 500 nautical miles southwards from Yokohama. In 1830, five men of different nationalities came there with a number of Kanaka women from Hawaii and founded a colony. Some of them left or died without offspring, so that only the American (Savory) remained, and he was soon made head of the colony. In the next decade others came, including an Englishman (Webb), a " Portuguese " from Cape Verde, a mulatto, another Englishman, and a negro from Bermuda. All the women, however, were Polynesians from Hawaii, Guam, or Ponape. About 1860 the Japanese began to arrive, and they now number 2,000 on the small islet of Chichijima. The older generation, descendants of the early settlers, have an Anglican church, speak English, and keep to themselves, but are now dying out, while the younger generation is marrying the Japanese, and they no longer speak English. About sixty of the pre-Japanese descendants are left. They are mostly F_1, F_2, and F_3, from English men crossed with Polynesian women. There are now all possible mixtures of whites, negroes, Polynesians, and Japanese.

Of the Savory F_1 from a Polynesian woman from Guam married to an American, three are still living. They are about seventy years of age, large, nearly European in visage, but a little foreign as regards the nose and cheek-bones. The skin colour is scarcely darker than that of a white man in the tropics. They all in youth had jet-black hair and eyes. Now in old age their hair is flaxen (not white) and their eyes grey-blue. The old woman looks more like a mulatto than the men. Using P for Polynesian and W for white, another family had this descent:

$$[(P♀ \times W♂)♀ \times W♂]♀ \times (P♀ \times W♂)♂.$$

Hence this was nearly an F_2, and the family showed segregation of characters. Jane was pure white, with white skin, chestnut hair, and European face. Another sister was similar but with darker skin; a brother had dark skin and might be mistaken for a Polynesian. He has a Japanese wife, and their child is indistinguishable from a Japanese child. The Japanese type is strongly dominant here, as it is in crosses with pure Europeans.

Another family is (P♀ × W♂)♀ × W♂. The children from this cross would be one-quarter Polynesian. The son appears fully white, the daughter (Kate Webb) has pretty European features and very good profile, but straight black hair and a very dark skin: hence clear segregation. In another case, the F_2 daughter from (P♀ × W♂)♀ × (P♀ × W♂)♂ was very much darker than her parents, nearly black, but her facial features more European than Polynesian. In a family with this descent—(P♀ × W♂)♀ × N♂ (negro)—the two sons both have woolly hair, but one (Rufus) is fully like a pure negro, while the other is like a mulatto, with lighter skin and negroid nose and lips.

Rufus married Kate Webb. Hence their offspring will be [(P♀ × W♂)♀ × W♂]♀ × [(P♀ × W♂)♀ × N♂]♂. One of their two children who were seen was a son with the curly hair, dark skin, and thick lips of a negro; the daughter had a mixture of characters of the three races, thick shining black hair, dark skin, European nose, and very slightly thickened lips.

The "Portuguese" settler mentioned above had mulatto blood. His son by an Hawaii woman was a good-looking "Portuguese" mulatto with very dark skin, who married a woman (P × W)F_1. The only son seen was the Rev. José, in whom the original negro characters were clearly visible. He had very wavy hair, medium skin colour, rather thick lips, and high cheek bones, but European nose. He married a Japanese woman. The whole pedigree would thus be represented:

[(P♀ × (W♀ × N♂)♂)♂ × (P♀ × W♂)♀]♂ × J♀.

Their three children were extraordinarily different. A daughter is fully Japanese, of clear and pretty Japanese type. A son is strongly Japanese, but with a touch of European features. Another son is nearly negro: curly hair, thick lips, broad nose, but skin medium brown. Another daughter (not seen) was similar but less negroid.

In another family involving white, negro, and Polynesian ancestry, one daughter (Eliza) had practically European features, but light brown skin and slightly wavy hair. The other daughter had somewhat European features, but purely negro hair and very dark skin. The latter married a Japanese, and their four children were as follows: Dorothy, half negroid, with curly hair and dark skin, but more Japanese features;

Betty, rather Japanese type, but somewhat dark skin, slightly wavy hair, but rather European features. The other two girls were nearly like Japanese, but had somewhat darker skin, and one had clearly negroid nose and mouth. Eliza (above) married two different Germans. Their children appeared to be of pure European type, but the hair of the elder daughter betrayed her origin.

English traditions were upheld throughout these mixtures of such different races. The negro characters are evidently strongly dominant, as are the Japanese, and the numerous segregations are very striking.

Another example of racial crossing under conditions of isolation is on the island of Tristan da Cunha, but little appears to be known of the present racial composition or appearance of the inhabitants. This group of three small volcanic islands in the South Atlantic, only one of which is inhabited, was discovered in 1506, but its permanent habitation only began in 1810. In 1827 five coloured women, presumably of mixed ancestry, from St. Helena, migrated to Tristan and became the wives of Britons already there. Other coloured women came later from Cape Colony. In 1846 a Dutchman was wrecked on the island; in 1856 two Americans joined the party there; and in 1882 two Italian sailors landed there. Thus the descent is chiefly from British men married to women of mixed negro ancestry. In 1857 forty-five of the inhabitants removed to Cape Colony, but the majority have not been tempted to emigrate from their island home. In 1880 the population reached 109, but through various disasters it was reduced to 64 in 1897, and it is now said to be about 140, of whom 69 are adults. The evidence of coloured ancestry was marked in the older inhabitants, but few of the present adults and very few of the children are said to show evidence of such ancestry. A survey of the present population would make an interesting study in "dilution" through continued crossing with whites. The population is increasing, their health is good, and there are no signs of degeneration from intermarriage. Dental caries is rare. Although there is no currency, the property is gradually passing into the hands of a few.

The Pitcairn Islanders have a more romantic history. They are descended from English sailors, who mutinied on the voyage of the *Bounty* to Tahiti in 1788, and with native Polynesians formed a colony on the little tropical island of Pitcairn, whose area is only two square miles, in the mid-Eastern Pacific.

A picturesque account of the voyage, the mutiny, and the early history of the colony is edited by an anonymous writer (1839). The *Bounty* had been commissioned to introduce the bread-fruit tree from Otaheite to the West Indies. The mutiny took place after leaving Tahiti with their cargo of bread-fruit trees. The mutineers took charge of the ship and returned to Tahiti. Nine of the sailors here took Polynesian wives and sailed to Pitcairn with six Otaheitan men-servants, where the ship was run ashore and burnt. Another statement (p. 286) says there were eight English sailors and eighteen Polynesians, six men and twelve women. Four years later the Otaheitans killed every Englishman except Alexander Smith, whom they severely wounded, and the same night their widows killed all the Otaheitans, thus leaving Smith as the only man, with eight or nine women and several small children. In 1808, when the colony was discovered by a passing ship, they numbered about thirty-five, spoke English, and were being brought up to lead exemplary lives.

This population, descended from white men and Polynesian women, numbered 194 in 1856, when they were landed on Norfolk Island. Two years later two families returned to Pitcairn, followed by a few others (forty in all) soon afterwards. In the 1870's the resulting colony was in good order, but by 1900 deterioration of intellect and morals had occurred, which was attributed to intermarriage. The population of the two islands reached about 1,000 at one time. Hermann (1901) has also described these people.

Haecker (1911, p. 247) cites the statement of Townsend that the Pitcairn Islanders (Tahitian ♀ × English ♂) in F_1 have all (with one exception) dark hair, dark eyes, and olive skin. In F_2 some are as dark as full-blooded Tahitians, others as light as Europeans, and both types appear in the same family.

As reported by Hooton (1926), Dr. Shapiro set out from Harvard University in 1923 to make an anthropological study of the present Pitcairn and Norfolk Islanders. He found about 400 on Norfolk Island and 175 on Pitcairn. No deterioration from inbreeding was to be observed, but hybrid vigour showed in certain characters. They were found to exceed the parent stocks in stature, and their head diameters were among the largest in any people, with a tendency to dolichocephaly. Their features were predominantly European, but a hybrid type of nose is often seen. The hair is usually very dark and the skin colour between that of a European brunette and the

brown Polynesians. They show much variability, and more curly hair than among either the British or Tahitians. Full results will no doubt be published later.

In Hawaii more races have been involved in crossing than perhaps anywhere else. Hoffman (1923) states that the population was 130,313 in 1832, diminished to 56,879 in 1872, and had increased to 255,912 in 1920. In the present population forty-one countries are represented, yet racial mixture is much more restricted than is generally assumed. But all foreigners, when they intermarry, show a preference for Hawaiian women. There is not promiscuous racial mixture. Dunn (1923), in an investigation of the Hawaiians and their crosses, finds the commonest triracial cross to be white-Hawaiian-Chinese. The hybrids are intermediate in measurements and no hybrid vigour is shown. A few Hawaiians have red hair, and it is uncertain whether this has come from early crosses with Europeans or is of independent origin. The Hawaiian hair is usually wavy or curly, but occasionally frizzy, crinkly or kinky, perhaps from negro or negrito mixture. Some have straight hair but less coarse than in Mongols. In crosses with the Chinese (smooth, coarse, straight hair) the F_1 had the Mongolian type of hair in 18, wavy in 8, curly in 1, and wiry in 1. In F_2 both types of hair appear. In $F_1 \times$ Hawaiian, 19 had wavy or curly hair, 9 straight, where a ratio of 1 : 1 might be expected. In one such family, 5 had curly hair and 3 straight.

The Mongolian eye-fold is present in 80 per cent. of the population of Southern China and in only 2·5 per cent. of Hawaiians. In the F_1 cross it was found in 35·7 per cent. (28 individuals), thus indicating incomplete or variable dominance. In $F_1 \times$ Hawaiian there were 14 with the fold to 14 without it, which would be in conformity with a single-factor difference. But $F_1 \times$ Chinese gave 3 with the fold and 2 without it. In general, the F_1 of crosses between Chinese and Hawaiians is more like the Chinese, who appear to have more dominant factors than the Hawaiians.

Saller (1927) points out that red hair is well known in the Malay Archipelago. E. Fischer has described red-haired natives of New Guinea and Melanesians, in whom it appears to have had an independent origin from that of the white man. Small blond-haired groups also occur. Rodenwaldt (1927), who has studied the natives of Kizar, a small island in the Malay Archipelago, gives several pedigrees of individuals with black hair and red beard. In a general discussion of rutilism,

Saller concludes that it is at present impossible to form a certain theory of the formation of the red and brown pigments, and of the inheritance of these conditions. Rodenwaldt, however, concludes that red hair is a Mendelian recessive.

Dunn (1928) has made a considerable anthropometric study of the Polynesians of Hawaii and their crosses with numerous races, including Europeans, Chinese, Japanese, Koreans, Portuguese, and negroes. In all, 508 subjects were measured, a third of whom were pure Hawaiians. The bodily dimensions of Europeans and Hawaiians are similar, except for the greater corpulence of the latter. Whether this is inherited as a dominant or is due to diet and habits of life is uncertain. The brachycephalic head shape of the Hawaiians is found to be dominant in later hybrid generations. The broader nose of the Hawaiian appears in the F_1, and is possibly due to dominant factors, while the high and narrow root of the nose in Europeans is dominant to the depressed base of the Hawaiian nose. Broad nostrils and high root of the nose appear together in some F_1 hybrids. It is believed that the differences between the two types of noses represent but few factors.

The darker hair colour, more wavy hair, and darker eyes and skin of the Hawaiian type are partially dominant; and straight hair, blond hair, eyes and skin may appear as recessives in later generations from a cross. Hawaiians appear to contribute more dominant factors to a cross than Europeans, although the dominance is usually incomplete. Clear evidence of segregation in the F_2 and the backcross generations is found as regards the racial characters, such as nose and head form, hair and skin colour.

The conclusion is reached that the chief divergencies between Hawaiians and Europeans are in the more Mongoloid features of the Hawaiians. There appear to be fewer differences between the Hawaiian and European types than between Hawaiian and Chinese, so that Hawaiians are regarded as occupying a place intermediate between Europeans and Mongoloids, but nearer to the former in affinity. The number of heritable differences between these races appears to be small when their long geographic isolation is considered. But none of these races is uniform, and the term race as applied to a congeries of physical characters can only be used in a relative sense. The crossing of these races in Hawaii produces a heterogeneous population, in which the races do not segregate as such, but individuals with many recombinations of the

various racial traits appear. The ultimately preponderating characters of such a population will depend not only on the original ingredients, but also upon the environmental forces, and perhaps still more on the processes of sexual selection acting upon later generations.

Malcolm (1920) describes the results of crosses between Tasmanian natives and Europeans. Stephens (1898) has contributed some notes on their history. Several sealers and escaped convicts took Tasmanian wives on Cape Barren Island, midway between Tasmania and Australia, as early as 1797, and from this source the present population of this island is descended. There was also a party of aboriginals, deported from the mainland. The male progenitors included English, Irish, Scotch, Germans, Maoris, and Jews. The natives on the mainland of Tasmania were exterminated in 1835. Although the Tasmanian race is long since extinct, some of their blood survives in this population. As late as 1830 some fifty aboriginal women were kept in slavery by white men on these islands in Bass Strait. One European had thirteen children by an aboriginal woman. In 1851 some of the descendants from these crosses took part in the gold rush to Australia, and many honourable and prosperous families are descended from them.

The number of half-castes was estimated to be eighty or ninety in 1876, and in 1912 there were nine families on the island comprising about one hundred persons. Close intermarriage had taken place, and there were "signs of degeneracy, both mental and physical."

Stephens describes these people as living by the sea and refusing to go inland more than a mile, although Cape Barren Island is 25 miles long and 8 miles wide. Their bodies have a fishy odour from eating the sooty petrel, or mutton bird, which they catch in great numbers during a period of two months, remaining idle for the rest of the year.

In 1920 Malcolm found only two old men surviving, who claimed to be the sons of Tasmanian aboriginal mothers—*i.e.*, one-half Tasmanian. One, Captain P. Thomas (Fig. 80), who was the son of a mariner from Cardiff, was very intelligent, and held a master mariner's certificate. His cranial capacity was estimated at 1,594·5 c.c., eyes light brown, skin light brown, hair grey and curly. One of his sons married a quarter-caste Tasmanian, and they had three children. The eldest, aged ten, had entirely European features showing no aboriginal characters; her eyes were very light brown, hair ash-blond,

FIG. 80.—TASMANIAN × ENGLISH. (After Malcolm, from *Man*, vol. xx.)

FIG. 81.—⅛-TASMANIAN, WITH CLOSELY CURLED HAIR AND WHITE SPOTS ON THE SKIN. (After Malcolm, from *Man*, vol. xx.)

and she even spoke differently from the rest of the islanders. Her brother, on the contrary, had dark brown skin and eyes, hair almost black and slightly wavy. A descendant from a sister of Captain Thomas, who appears from the pedigree to be one-eighth Tasmanian (Fig. 81), shows the typical closely curled Tasmanian hair, and, like some others of the younger generation, "distinct evidence of absence of pigmentation on parts of the face and body." This spotting may be a "dilution effect" similar to that occasionally occurring in the descendants from mixed negro-white crosses (see p. 108). These crosses between Tasmanians and Europeans have been regarded by some as giving rise to Dravidian types unlike either parent race. The segregation in the descendants from this cross is striking enough, but it is difficult to say how much basis there is for the view that Dravidian types appear.

Davenport (1925), in a study of the Australian natives, finds that the F_1 hybrids with white men have a skin colour like that of the mulatto, but with the yellow element not so high. Topinard long ago concluded that the Australian aborigines were of two types: (1) tall, dolichocephalic, lighter skinned, straight haired; (2) more dolichocephalic, short, with black skin and frizzy or curly hair. Davenport discusses the question whether these differences have arisen as mutations on the Australian continent or whether they represent incursions from different races (Malayan and Papuan). He concludes that the Australians are Neanderthaloids rather than derived from Dravidians. They have probably the longest legs of any living race; their skin colour shows great variability, but is generally darker than the negroes of Jamaica or Bermuda. Their eyes are dark brown, hair dark brown or black, usually wavy, but may be straight or curly.

Miss Fleming (1926) has made a study of the children from a Chinese father and an English mother. Nearly half of them (number not given) had the Mongolian eye-fold. About 68 per cent had the Chinese skin colour and the characteristic "opaque" brown eyes of the father, while one had blue eyes and another different eyes, one with the Mongolian fold, orbit shape and eye colour, the other a light grey-brown English eye. Nearly half had the hair colour of the father, but in some it was intermediate, soft and silky, but straight. Over half had broad flat noses, and nearly half had broad lips like the Chinese. In 40 per cent. a curious conformation of the parietal bones characteristic of the Chinese was found. Only 15 per cent.

were brachycephalic like the Chinese, and some were markedly dolichocephalic, contrary to expectation. The children frequently showed ability, and no case of mental or moral deficiency was recorded.

A study of a hybrid population from crosses between Malayans and Europeans (chiefly Dutch and Portuguese) on the little island of Kizar, near Timor, has been made by Rodenwaldt (1927). On this small island in the Malay Archipelago, a hybrid population of several hundred has developed since 1750, and their descendants through six or seven generations have been studied. The conclusions are in general agreement with many others already given. The bodily characters of the mixed descendants are found without exception to show segregation. Dominance is regarded as occurring in the great majority of cases, but it should be recognised that the dominance is usually incomplete. As regards head dimensions, the broad European head is dominant, as well as the long face of the European. Similarly the large and long ear of Europeans; but as regards the teeth and their position, and perhaps the size of the chin, the Malayan condition is more or less dominant. Some of the Malayan nose factors are dominant, and the small European lips are recessive. The dark skin, hair and iris colour are of course dominant, and nothing was found against the view that smooth hair is recessive to curly. No phenomena of hybrid vigour were observed.

Crosses with Africans.

Crosses between negroes and whites have occurred in many countries over a long period, and an immense amount has been written on the subject, particularly in America, but until recent years the subject remained a sterile one so far as scientific analysis of racial crossing is concerned. Hrdlička (1927) has published a comprehensive bibliography of the anthropology of the American negro, with a brief account of what has been done.

Skin colour and its inheritance has received much more attention than any other physical feature of the negro, because it is obvious and its variations are easily observed. Indeed, depth of skin colour is generally but quite erroneously regarded as a true criterion or measure of negro-blood, whereas a man of mixed ancestry may have a white skin combined with negroid features, or a dark skin and otherwise "white" features.

The percentage of American negroes with one or more white ancestors is probably much larger than is generally supposed, and some anthropologists hold that few if any negroes of pure-blooded ancestry remain in America.

Davenport (1913) was the first to suggest that two factors for skin colour are involved in negro-white crosses, but much work has been done since then in America, South Africa, and England. Hoffman (1923) describes the results of intermarriages in Minnesota between poor white women and the better type of negro men. These women are mostly of foreign origin. In one family the mother was German, while the father had negro and Indian blood. The two girl children had chocolate-coloured complexion and woolly hair, which was sandy red like the mother. Their lips were thin, but eyes and nose negroid. Two hundred such mixed families are believed to exist in the Twin Cities, Minneapolis and St. Paul. Many in later generations pass successfully as whites although having coloured blood. Such intermarriages are regarded as anti-social and opposed to sound eugenics, but they evidently constitute a considerable element of the lower strata in the Northern cities of the United States.

Davenport (1928) has made a further study of race crossing in Jamaica, 98 per cent. of whose population is coloured. One hundred each of pure blacks, pure whites and browns or hybrids, living under the same conditions, having the same education and occupation (farming), and belonging to the same social stratum, were selected for study. Strong evidence of a constitutional genetic difference between the two races both physically and mentally was obtained. The browns were intermediate in nearly every respect, although they live side by side with the blacks. In discrimination of pitch and rhythm, using the Seashore tests, the blacks were found to be better than the whites, but there was no certain difference in sense of harmony. In tests involving some organisation and planning, and in those involving common sense or logical faculty, the blacks were inferior. The browns were precocious, scoring higher than whites or blacks at the age of ten to sixteen years, but as adults they were worst of all in the intelligence tests, though showing much variation. Crossing of the races thus produces many ineffective, disharmonious individuals, but a few superior ones.

In physical characters, the negroes have longer arms and legs, narrower pelvis, longer head, eyes wider apart, feet and

hands longer, ears shorter and rounder, with fewer and shorter hairs on the hands, arms, and legs. They also show less dental caries up to sixteen years, but more afterwards.

Herskovits (1927, 1928) developed at some length the theory that American negroes of mixed descent are no more variable than the pure parental races. This is impossible to credit as regards skin colour, where every shade is seen from nearly white to quite black. Herskovits actually found the mulattoes less variable in stature than whites, but whites and negroes have the same mean stature. Davenport points out that this relatively low variability of the mixed breeds applies only to traits in which the races do not differ. In nose breadth, for instance, the F_1 is intermediate, but later generations show great variation. In whites this feature measures 30-41 mm., in blacks 40-53 mm., while in browns it ranges from 33-53 mm.

Steggerda (1928), in a continuation of these studies in Jamaica, made six measurements on each of 1,400 school children belonging to the black, white, and brown groups. He found the arms and legs shortest in the whites, longest in the blacks, and intermediate in the browns. The chest girth was the same in all three groups, while the black children had slightly greater height and weight. White children had the longest trunk, blacks the greatest head length, and the browns were intermediate in every measurement in which the white and black groups differed. In further studies, reported in Carnegie Year Book, No. 27 (1928), Steggerda finds that the long-legged condition of the blacks is probably present from birth onwards, and not due to the persistence of the condition found in twelve-year-old whites. At birth, black babies weigh less and have smaller heads than whites. The variability of the hybrid browns is found to be greater than that of the parent stocks just in those characters in which the races differ in simple genetic fashion. In papillary patterns the negroes show 50 per cent. more whorls, while radial loops are much rarer than in whites.

From extensive statistics, Holmes (1928*a*) finds that the American negro is relatively immune to skin diseases and scarlet fever, diphtheria and (to a less extent) measles. This is believed to be due chiefly to his more resistant ectodermal structures. He also concludes (1928*c*) that the negro was formerly dying out through high infant mortality, but that in the northern cities he may be now adapting himself so as to increase in the future.

Miss Fleming (1926), in mixed crosses between negro men and white women in English seaport towns, records cases of negro skin combined with flaxen hair, or negroid colouring with black woolly hair and very white scalp. In another the eyes and lips were English, the hair dark, scalp very light, skin colour a rich brownish red. Characters of eye, skin, hair, and lips are thus inherited with some degree of independence. A number showed mental deficiency inherited from the mother. There is nothing to indicate that the reciprocal crosses are different, and this is not to be expected.

Miss Fleming is continuing her studies with Professor Fleure, and has kindly allowed me to quote from some of her unpublished results. Among the negro features regarded as characteristic are the " opaque " brown iris with a yellow stain in the eye-ball, slender bones and bulbous joints, strong eye ridges and widely spaced eyes, in addition to the usually recognised features. Steatopygy and prognathism also appear. Facial disharmony frequently results from crosses between a negro father and a white mother. The upper jaw may be widely arched and large with well-spaced teeth, the lower jaw small and V-shaped with crowded teeth, interfering with speech in some cases. In others the upper jaw may be small, with the lower teeth then resting against the upper lip.

Striking cases of segregation in the backcross were observed. (W×N) ♀ × ♂W gave a family of two children, one of whom had a yellowish skin with florid cheeks, eyes dark-grey brown with darker brown rays and flecks, hair dark brown, wavy. The other was of purely white type with fair, fresh skin, eyes like her sib, hair brown, wavy. One wonders in this case whether the original negro father was pure-blooded, but it is stated that the children from the F_1×W♂ would usually pass for white. The F_1 crossed with black gave, in one family of thirteen, children with brown or dark brown skin, all but two having opaque dark brown eyes, these two being brown and dark brown respectively. In hair characters, eleven (including the last two) had typical black woolly hair, one had straight black hair, and one straight, very dark brown hair.

In another family from F_1×N, four children were markedly prognathous (the nose was mostly broad and flat), two had both lips thick and everted, while one had the lower lip everted and the upper long. In two cases there was disharmony of the upper and lower jaws. Four children are described from (English ♀ ×Arab ♂) ♀ ×negro♂. One had some wavy and

some very tight curly hair, the second had very tight curls, the third straight hair, and the fourth wavy hair. Two had tremulous thick everted lips, and one of these showed steatopygy. Three had dusky brown skin with golden red in the face, one had light brown skin.

Among eighty children from negro-white crosses, all but one had coloured skins; 91 per cent. had woolly hair, eight had brown or very dark brown hair of English type, while one had flaxen woolly hair in infancy, becoming black at three years of age; 72 per cent. had opaque eye, 70 per cent. had broad flat noses, and 20 per cent. had everted lips, 60 per cent. having slender limbs and bulbous joints.

In South Africa, where crossing has long taken place, producing the Cape Coloured people, studies of racial crosses have recently been made by Fantham (1925), and more extensively by Lotsy (1928). Fantham describes a cross between a Zulu woman and a Belgian with blue eyes and fair hair. Of the eight children, two were classed as "white," three "black," and three "brown." The eldest daughter, who was black, married a Zulu from Natal. Two of their sons were classed as black and two brown. The white daughter married a Zulu, and they had a "black" son and a "white" daughter. If the original Zulu woman were heterozygous, then these striking results in segregation might be explained. In any case, segregation in these crosses seems much freer than in the many crosses observed in America, where a different negro race is involved. The white and black sibs are said to despise each other, and both despise the brown. In a Johannesburg family, four generations are descended from a Dutchman and a native woman. Among them is a man with blue eyes, white curly hair, and somewhat thick lips.

Lotsy (1928) gives a considerable history of racial movements and crosses in South Africa. The Cape Coloured are a people resulting from early crosses between the Dutch and Hottentots, Bantus and Malay slaves, beginning as early as 1666. They form nearly half the population of Cape Town, and are a hybrid race. They have a definite physical type with a characteristic accent and laugh. They associate together and marry together, speaking Afrikaans, a hybrid language. They often have the oval face and straight, coarse black hair of the Malay.

Throughout Africa was a region of tribal warfare and racial mixture, the defeated tribe being held in slavery or killed and

their women taken as wives. Huxley originally suggested that the Hottentot race resulted from a mixture of Bushmen with Bantu, and that still remains a possibility. Lotsy, who regards crossing as universal in the human race, suggests the following mixed relationships in South Africa (Fig. 82):

```
                                 Bushmen × Bantu
                                          |
                                          ↓
(Malay + Hottentot) ×  White  ×  Hottentot ?          × Bantu
                    |          Masarwa
                               Gonaqua (in part)        |
                    ↓        ↓                          ↓
                 Cape     Rehoboth                Berg-Damara
              Coloured    Bastaards               Korana (in part)
```

FIG. 82.—HYBRID RACES IN SOUTH AFRICA

The Bantu swept over vast areas of Central Africa, assimilating other peoples. The clicks in the Bantu languages such as Kaffir were imported from the Bushmen and Hottentots. When the Kaffirs made war they killed the men and kept the women, the latter clinging to their kitchen language, which is full of clicks and became absorbed into the language of the conquerors. Lotsy cites numerous other cases of hybrid tribes and peoples in South Africa.

As regards segregation, in crosses between the Basuto (a branch of the Bantu) and Bushmen it is relatively common, some of the segregates being almost like the Bushmen, with dwarf stature, hair in tufts, no ear lappet, high cheek-bones, and broad skull. Lotsy suggests that Bushmen and Bantus crossed with the Central African pygmies in an earlier period, and that the recessive dwarfing now segregates as a single factor. In a family in which the mother was tall and the father short, five of the children were short and three tall, indicating a 1 : 1 ratio, with the mother heterozygous for tallness.

A very striking case of segregation in skin colour is described. A woman whose father was English and mother Basuto had brown yellow skin, brown eyes, and Basuto hair (Fig. 83). She married a white man with brown eyes and straight dark brown hair. Their two sons were both quite white, with eyes like the father and straight brown hair. That the only two children from this backcross should have a complex of white characters is difficult to harmonise with any theory of the independent segregation of multiple factors for skin colour and

hair characters. Evidently, close linkage of the recessive factors involved must be assumed in this case. Even so, the amount of segregation is much in excess of anything ever described in American negro crosses. One would suppose, however, that the longer period of crossing in America would have led, through diminution of the duplicate factors, to the

FIG. 83.—SEGREGATION IN ENGLISH-BASUTO CROSSES. SEE TEXT. (After Lotsy.)

more frequent occurrence of pure white segregates there than in Africa. Perhaps South African natives have single factors for skin colour, eye colour, and hair characters.*

* That a real genetical difference as regards skin colour exists between South African natives and the negroes of America, whose ancestors came from West Africa, is confirmed by the following quotation from Darwin (*Descent of Man*, p. 197): " Dr. Rohlfs informs me that he has frequently seen in Africa the offspring of negroes crossed with members of other races, either completely black or completely white, or rarely piebald. On the other hand, it is notorious that in America mulattoes commonly present an intermediate appearance."

One other case from Lotsy may be cited, showing segregation of the more usual type in skin colour, but more marked as regards hair characters. A Griqua woman married a Scot. The daughter, who married a white man, was no darker in skin pigmentation than a white woman would be who was living under the same climatic conditions in the open in south Africa; but if she had lived indoors she would have had a pale yellow skin.* Four of their sons are shown in Figs. 84 to 87. John (Fig. 84) is almost white, very tall, with brown eyes and frizzy hair. James (Fig. 85) is of medium height, with a darker skin, long, straight, black hair and brown eyes. Joseph (Fig. 86) is of medium height with darker yellow skin than James, more Kaffir-like hair, eyes brown. Richard (Fig. 87) is of medium height, with darker skin than John, brown eyes, and brown-black Hottentot hair.

Clearly, segregation is so abundant in South Africa that the observer cannot escape its recognition. It is also clear that the factors for skin colour in South Kaffirs must be fewer than, or different from, those in the negro. Perhaps a single factor for black pigment is present.

Other Crosses.

An account of a probably unique relationship between two races which have intercrossed for centuries is given by von Eickstedt (1927). The Kandyan dynasty of Ceylon has been for several centuries the oldest in the world. Several of its ancestors were Veddas, the native aborigines. Formerly crosses took place between this primitive wild race and the highly civilised Singhalese. There is some evidence that the Veddas became somewhat civilised and afterwards relapsed. Until last century they were supports of the Kandyan dynasty as palace guards and war troops. A kind of symbiosis developed between the races, the Veddas having high social position although biologically very primitive—"pseudo-australoid." Two of the Singhalese noble families are traced through six and seven generations respectively from crosses with Veddas. The modern members show some of the Vedda type, some Singhalese type, and some mixtures.

When any human race or population is analytically studied it is found to be composed of different elements more or less

* Personal communication from Professor Lotsy.

FIG. 84.—JOHN MACDONALD. SEE TEXT. (After Lotsy).

FIG. 85.—JAMES MACDONALD. *Cf.* FIGS. 84-87. (After Lotsy.)

FIG. 86.—JOSEPH MACDONALD. (After Lotsy.)

FIG. 87.—RICHARD MACDONALD. (After Lotsy.)

FIGS. 84-87 ARE BROTHERS.

inextricably mixed. It is therefore impossible to draw any sharp line between a pure race and a hybrid people, because every intergrade of condition exists. The analysis of even such a relatively pure race as the Swedes, therefore, differs only in degree from that of hybrid populations such as we have been studying, and it can yield results of great value in the understanding of human inheritance. Among the best of such racial studies are those undertaken by the Swedish State Institute for Race Biology at Uppsala, under the direction of Dr. Lundborg. *The Racial Characters of the Swedish Nation*, by Lundborg and Linders (1926), is a model anthropological study, elaborately illustrated, of the Swedish people, in which the Nordic, East Baltic, and Lapp races and their various intermixtures are recognised. The work is too extensive even to summarise here, but its outlook is entirely in harmony with the application of genetical analysis to racial characters.

Lundborg (1923) has also made a study of the Finns in Northern Sweden. The Finns and Swedes agree in being fair with blue eyes, but while the Swedes are dolichocephalic, the Finns are brachycephalic with high cheek-bones, belonging to the East Baltic race. The Lapps, on the other hand, have dark eyes and also are characterised by their nearly dwarf stature, dark hair, and flat oval face, with fair complexion, particularly in the women. On the basis of eye colour it is calculated that about one-third of the so-called Finn population of Northernmost Sweden is Lappic. About 30 per cent. are regarded as Nordic, the remaining 40 per cent. being pure Finns.

Mjöen (1923) has also made a study of the Lapps in Norway. He finds that many Lapps in this area have blue eyes, but none the pure blue of Middle Norway. Such blue eyes have no doubt been derived by crossing with Nordics or East Baltic peoples. Mjöen also gives light brown eyes and hair as characters of the Nordic race. The Lapp-Nordic cross is nearer the Nordic, but no further analysis of the cross was given. The Laplanders' characteristics are stated to be low stature, round skull, broad face, high cheek-bones, broad flat nose, yellow-grey skin, small uneven beard, dark oblique eyes, black straight hair, and Mongoloid features. The eye colours in 55 Laplanders from an encampment in Finmarken ranged from black-brown (4) and dark-brown (15) to greenish light blue (12) and blue with brown spots (17). Clearly, the Lapps now remaining in Northern Scandinavia and Finland have undergone much crossing with adjacent peoples.

Mjöen emphasises the disharmonic character of Nordic-Lapp crosses, which frequently give rise to mentally and physically unbalanced types. In addition to nine unbalanced cases, four were found in which the F_1 were taller than the parents and had a better mentality than the Lapps. Tuberculosis mortality is found to be lowest in parts of Norway where there is no racial crossing, and very high in Finmarken, where nearly half the population consists of Lapps, Kvens, and Finns.

LITERATURE

ANONYMOUS. 1839. The eventful history of the mutiny and piratical seizure of *H.M.S. Bounty*: its cause and consequences. 3rd edition. London: Murray, pp. 356.

ASHMEAD, A. S. 1905. The mulberry-coloured spots on the skin of the lower spine of Japanese and other dark races: a sign of negro descent. *Journ. Cutan. Diseases*, xxiii. 203-214.

BAHRAWY, ALI ALMED EL. 1922. Über der Mongolenfleck bei Europäern. *Arch. f. Dermat. u. Syph.*, cxli. 171-192, figs. 4.

BASLER, A. 1927. Über den Einfluss der Lagerung von Säuglingen auf die bleibende Schädelform. *Zeits. f. Morph. u. Anthrop.*, xxvi. 225-246, figs. 19.

BEAN, R. B. 1908. Heredity of hair form among Filipinos. *Amer. Nat.*, xlv. 524-536.

VAN BEMMELEN, J. F. 1928. Die Vererbung der Haarform beim Menschen. *Verh. V. Internat. Kongr. Vererb.*, i. 408-421, figs. 12.

BOAS, F. 1912. Changes in bodily form of descendants of immigrants. Columbia University Press, pp. 573.

BOAS, F. 1920. The anthropometry of Porto Rico. *Amer. Journ. Phys. Anthrop.*, iii. 247-253.

BOND, C. J. 1912. On heterochromidia iridis in man and animals from the genetic point of view. *Journ. Genetics*, ii. 99-129, pls. 4, figs. 7.

BRENNEMANN, J. 1907. The sacral or so-called "Mongolian" pigment spots of earliest infancy and childhood, with especial reference to their occurrence in the American negro. *Amer. Anthropologist*, ix. 12-30, pl. 1.

BROCA, PAUL. 1864. *The phenomena of hybridity in the genus Homo.* With report of the Anthropological Soc. of London. London: Longman, Green, Longman and Roberts, pp. 76.

BRUCH, O. 1924. Mongolenfleck bei Missbildungen. *Monatsschr. f. Kinderheilk.*, xxviii. 199-206.

BRYN, H. 1920. Researches into anthropological heredity. II. The genetical relation of index cephalicus. *Hereditas*, i. 186-212.

CARR-SAUNDERS, A. M. 1922. *The population problem.* Oxford Press, pp. 516.

CATLIN, G. 1926. North American Indians. Edin.: John Grant, 2 vols.

CREW, F. A. E. 1923. The significance of an achondroplasia-like condition met with in cattle. *Proc. Roy. Soc. B.*, xcv. 228-255, pls. 4.

CREW, F. A. E. 1924. The bull-dog calf: a contribution to the study of achondroplasia. *Proc. Roy. Soc. Med.*, xvii. 39-58, figs. 15.

CREW, F. A. E. 1926. An achondroplasia-like condition in the sheep. *Vet. Journ.*, lxxxii. 598-601, figs 2.

DAVENPORT, G. C. and C. B. 1908. Heredity of hair-form in man. *Amer. Nat.*, xlii. 341-349.

DAVENPORT, G. C. and C. B. 1909. Heredity of hair colour in man. *Amer. Nat.*, xliii. 193-211.

DAVENPORT, C. B. 1913. Heredity of skin colour in negro-white crosses. *Carnegie Inst. Wash. Publ.*, No. 188, pp. 106, pls. 4.

DAVENPORT, C. B. 1917. The effects of race intermingling. *Proc. Amer. Phil. Soc.*, lvi. 364-368.

DAVENPORT, C. B. 1925. Notes on physical anthropology of Australian aborigines and black-white hybrids. *Amer. Journ. Phys. Anthrop.*, viii. 73-94.

DAVENPORT, C. B. 1928. Race crossing in Jamaica. *Sci. Monthly*, xxvii. 225-238, figs 11.

DUNN, L. C. 1923. Some results of race mixture in Hawaii. *Eugenics, Genetics, and the Family*, ii. 109-124.

DUNN, L. C. 1928. An anthropometric study of Hawaiians of pure and mixed blood. *Papers of the Peabody Museum, Amer. Archeol. and Ethnol., Harvard Univ.*, xi. 89-211.

EICKSTEDT, E. V. 1927. Rassengeschichte einer singhalesisch-weddaischen Adelsfamilie. *Arch. f. Rassen. u. Gesells.-Biol.*, xix. 369-388, pls. 7.

EPSTEIN, A. 1906. Über den blauen Kreuzfleck und andere mongoloide Erscheinungen bei Europäischen Kindern. *Jahrb. f. Kinderheilk*, lxiii. 60-73.

FANTHAM, H. B. 1925. Some factors in eugenics, together with notes on some South African cases. *S. African Journ. Sci.*, xxii. 400-424, figs. 4.

FISCHER, E. 1913. Die Rehobother Bastards und das Bastardierungs Problem beim Menschen. Jena: pp. 327, pls. 19.

FISCHER, E. 1923. Schädelform und Vererbung. *Münchener Med. Wschr.*, 1475.

FISCHER, E. 1926. Betrachtungen über die Schädelform des Menschen. *Zeits. f. Morph. u. Anthrop.*, xxiv. 37-45.

FLEMING, R. M. 1926. Anthropological studies of children. *Eugen. Rev.*, xviii. 294-301.

FRETS, G. P. 1917. On Mendelian segregation with the heredity of head-form in man. *Proc. Roy. Acad. Sci. Amsterdam*, xx. 435-865.

FRETS, G. P. 1920. De polymerietheorie getoetst aan de erfelijkheid van den hoofdvorm. *Genetica*, ii. 115-136.

FRETS, G. P. 1921. Heredity of head-form in man. *Genetica*, iii. 193-384.

FRETS, G. P. 1924. Heredity of the cephalic index. 's-Gravenhage: Nijhoff.

FUJISAWA, K. 1905. Sogenannte Mongolenflecke der Kreuzhaut bei Europäischen Kindern. *Jahrb. f. Kinderheilk.*, lxii. 221-224.

GATES, R. R. 1926. Mendelian heredity and racial differences. *Journ. Roy. Anthrop. Inst.*, lv. 468-482.

GATES, R. R. 1927. *A Botanist in the Amazon Valley.* London: Witherby, pp. 203, figs. 23 and map.

GATES, R. R. 1929. Blood groups of Canadian Indians and Eskimos. *Amer. Journ. Phys. Anthrop.*, xii. 475-485.

GATES, R. R. 1929. A pedigree study of Amerindian crosses in Canada. *Journ. Roy. Anthrop. Inst.*, lviii. 511-532, pls. 5, pedigrees 6.

GAUTIER, P. 1925. A propos de la tache bleue mongolique en Suisse. *Rev. Méd. de la Suisse Romande*, xlv. 301-303.

GODDARD, H. H. 1917. Mental tests and the immigrant. *Journ. Delinquency*, ii. 243-278.

GOLDSCHMIDT, E. 1927. Die Nachkommen der alten Siedler auf den Bonininseln. *Die Naturwissenschaften*, xv. 449-453, fig. 1.

GOSSAGE, A. M. 1908. The inheritance of certain human abnormalities. *Quart. Journ. Med.*, i. 331-347.

HADDON, A. C. 1919. *The Wanderings of Peoples.* Cambridge Univ. Press, pp. 124.

HADDON, A. C. 1924. *The Races of Man and their Distribution.* Cambridge Univ. Press, pp. 184, pls. 10.

HAECKER, V. 1911. Die Hapsburger Unterlippe. *Verh. d. Deut. Zool. Gesells.*, 109-113.

HAECKER, V. 1911. Die Familientypus der Hapsburger. *Zeits. f. Abst. u. Vererb.*, vi. 61-89, figs. 12.

HAECKER, V. 1911. *Allgemeine Vererbungslehre.* Braunschweig: Vieweg, pp. 392, figs. 135.

HAECKER, V. 1918. Die entwicklungsgeschichtliche Vererbungsregel in der Völkerkunde. *Zeits. f. Abst. u. Vererb.*, xix. 73-78.

HAECKER, V. 1918. Entwicklungsgeschichtliche Eigenschaftsanalyze (Phänogenetik). Jena: Fischer, pp. 344.

HAGEN, B. 1906. Kopf und Gesichtstypen ostasiatischer und melanesischer Völker. Stuttgart:

HANSEN, SØREN. 1893. Bidrag til Vestgrönlaendernes Anthropologi. *Medd. om Grønland*, vii. 165-253, pls. 8.

HERMANN, R. A. 1901. Die Bevölkerung der Insel Pitcairn. *Petermann's Mitteilungen*, xlvii.

HERSKOVITS, M. J. 1927. Variability and racial mixture. *Amer. Nat.*, lxi. 68-81.

HERSKOVITS, M. J. 1928. The American negro. A study in racial crossing. New York: A. A. Knopf, xiv. 92 pp.

HILDÉN, K. 1925. Zur Kenntnis der menschlichen Kopfform in genetischer Hinsicht. *Hereditas*, vi. 127-146, figs. 3.

HILDÉN, K. 1926. Die Runö-Schweden in anthropologischer Hinsicht. *Fennia*, xlvii. pp. 56, figs. 7, maps 2.

HILDÉN, K. 1927. Zur Frage von der ostbaltischen Rasse. *Acta Geographica*, i., No. 3, pp. 24.

HOFFMAN, F. L. 1923. Race amalgamation in Hawaii. *Eugenics, Genetics, and the Family*, ii. 90-108.

HOFFMAN, F. L. 1923. The problem of negro-white intermixture and intermarriage. *Eugenics, Genetics, and the Family*, ii. 175-188.

HOLMES, S. J. 1928*a*. The resistant ectoderm of the negro. *Amer. Journ. Phys. Anthrop.*, xii. 139-153.

HOLMES, S. J. 1928*b*. Age at parenthood, order of birth and parental longevity in relation to the longevity of offspring. *Univ. Cal. Publ. Zool.*, xxxi. 359-375.

HOLMES, S. J. 1928*c*. Will the negro survive in the North? *Sci. Monthly*, xxvii. 557-561.

HOOTON, E. A. 1923. Observations and queries as to the effect of race mixture on certain physical characteristics. *Eugenics, Genetics, and the Family*, ii. 64-74.

HOOTON, E. A. 1926. Progress in the study of race mixtures, with special reference to work carried on at Harvard University. *Proc. Amer. Phil. Soc.*, lxv. 312-325, fig. 1.

HRDLIČKA, A. 1927. The Neanderthal phase of man. *Journ. Roy. Anthrop. Inst.*, lvii. 249-274, pls. 4, figs. 5.

HRDLIČKA, A. 1927. Anthropology of the American negro. Historical notes. *Amer. Journ. Phys. Anthrop.*, x. 205-235.

HURST, C. C. 1912. Mendelian heredity in man. *Eugenics Rev.*, pp. 25, figs. 6.

JENNESS, D. 1921. The blond Eskimo. *Amer. Anthrop.*, xxiii.

JOCHELSON, W. 1928. Peoples of Asiatic Russia. *Amer. Mus. Nat. Hist.*, pp. 277, figs. 52, maps 10.

JORDAN, H. E. 1911. A comparative microscopic study of the melanin content of pigmented skins, with special reference to the question of colour inheritance among mulattoes. *Amer. Nat.*, xlv. 449-470, figs. 3.

KEITH, SIR A. 1920. The differentiation of mankind into racial types. *Rept. Brit. Assoc.*, Bournemouth, 275-281.

KEITH, SIR A. 1922. The evolution of human races in the light of the hormone theory. *Johns Hopkins Hosp. Bull.*, xxxiii. 155-159, 195-201.

KEITH, SIR A. 1929. The evolution of the human race. *Journ. Roy. Anthrop. Inst.*, lviii. 305-321, pl. 1.

KIRKCONNELL, W. 1925. Mendelism and cephalic index. *Amer. Journ. Phys. Anthrop.*, viii. 443-444.

LARSEN, NILS P., and GODFREY, L. S. 1927. Sacral pigment spots, a record of seven hundred cases with a genetic theory to explain its occurrence. *Amer. Journ. Phys. Anthrop.*, x. 253-274, figs. 16.

LITTLE, C. C. 1919. Some factors influencing the human sex-ratio. *Proc. Soc. Exptl. Biol. and Med.*, xvi. 127-130.

LOTSY, J. P. 1928. Hybridization among human races in South Africa. *Genetica*, x. 131-315, pls. 2, figs. 153.

LUNDBORG, H. 1920. Arv och miljö. Befolkingspolitiska synpunkter. *Det nya Sverige*, xiv. 3-12.

LUNDBORG, H. 1923. Racial structure of the Finns of the northernmost part of Sweden. *Hereditas*, iv. 125-132, figs. 4.

LUNDBORG, H., and LINDERS, F. J. 1926. The racial characters of the Swedish nation. *Anthropologia Suecica*, 1926, pp. 182, pls. 45.

LUS, J. 1927. Species-hybrids of *Bos taurus* and *Pœphagus grunniens* (Russian, English summary). *Bull. Bur. Genet. and Eugen.*, No. 5, pp. 39-78, pls. 4.

MACCAUGHEY, VAUGHAN. 1919. Race mixture in Hawaii. *Journ. Hered.*, x. 41-47, 90-95.

MALCOLM, L. W. G. 1920. Short notes on the inhabitants of Cape Barren Island, Bass Strait, Tasmania. *Man*, xx. 145-149, figs. 13.

MJÖEN, JON ALFRED. 1922. Harmonic and unharmonic crossings. *Eugen. Rev.*, xiv. 35-40.

MJÖEN, JON ALFRED. 1923. Harmonic and disharmonic race crossings. *Eugenics, Genetics, and the Family*, ii. 41-61, figs. 17.

NEUBAUER. 1925. Experimentelle Untersuchungen über die Beeinflussung der Schädelform. *Zeits. Morph. Anthrop.*, xxiii.

PEARL, M. D. and R. 1908. On the relation of race-crossing to the sex-ratio. *Biol. Bull.*, xv. 194-205.
PEARSON, K. 1909. Notes of the skin colour of the crosses between negro and white. *Biometrika*, vi. 348-353, pl. 1.
PERRIER, H. 1926. Un cas de tache sacrée bleue mongolique. *Rev. Méd. de la Suisse Romande*, xlv. 252-253.
REID, R. W., and MULLIGAN, J. H. 1925. Relation between stature, head length and head breadth of 847 natives of the North-East of Scotland. *Journ. Roy. Anthrop. Inst.*, liv. 287-299.
RODENWALDT, E. 1927. Die Mestizen auf Kizar. Batavia: Kolff and Co. 2 vols. Vol. i, pp. 483; vol, ii., plates, pedigrees, and diagrams.
RUHNAU, K. 1925. Einige anthropologische Angaben über die Bevölk erung der ostfriesischen Insel Spiekeroog. *Arch. f. Rassen. u. Gesells.-Biol.*, xvi. 378-381.
SALAMAN, R. N. 1922. Racial origins of Jewish types. *Trans. Jewish Hist. Soc. Engl.*, ix. 163-184, pls. 12.
SALAMAN, R. N. 1925. What has become of the Philistines? *Palestine Explor. Fund. Quart. Statement*, pp. 20, figs. 4.
SALLER, K. 1927. Erblicher Rutilismus in der Malayischen Inselwelt mit allgemeinen Bermerkungen über erbhang der menschlichen Haarfarbe. *Zeits. f. Abst. u. Vererb.*, xlv. 202-231, figs. 7.
SCHOHL, A. 1913. Über den sogenannten Mongolenfleck. *Zeits. f. Kinderheilk. Ref.*, iv. 145-162.
SCHREINER, ALETTE. 1924. Zur Erblichkeit der Kopfform. *Genetica*, v. 385-454.
SEDGWICK, W. 1863. On the influence of sex in hereditary disease. *Brit. and Foreign Med.-Chirurg. Rev.*, xxxi. 445-478, xxxii. 159-197.
SELIGMAN, C. G. 1904. Congenital cretinism in calves. *Trans. Path. Soc. Lond.*, lv. 1-20, figs. 6.
STEGGERDA, MORRIS. 1928. Physical development of negro-white hybrids in Jamaica, British West Indies. *Amer. Journ. Phys. Anthrop.*, xii. 121-138.
STEPHENS, E. 1898. The Tasmanian half-castes of the Furneaux Islands. *Journ. Manchester Geogr. Soc.*, xiv. 355-360.
SUK, V. 1928. On face types in man. *Anthropologie* (Prague), vi. 35-40.
SUK, V. 1928. Congenital pigment spots in Eskimo children. *Anthropologie* (Prague), vi. 28-34, pls. 2, figs. 4.
SULLIVAN, LOUIS R. 1920. Anthropometry of the Siouan Tribes. *Anthrop. Papers, Amer. Mus. Nat. Hist.*, xxiii. 81-174.
THOMSON, A. 1913. The correlations of the isotherms with variations in the nasal index. *17th Internat. Med. Congress*, xvii. pt. 2, 89-90.
THOMSON, A., and BUXTON, L. H. DUDLEY. 1923. Man's nasal index in relation to certain climatic conditions. *Journ. Roy. Anthrop. Inst.*, liii. 92-122, pl 1.
TOMESKU, I. 1928. Kongenitale Deviationen der Phalangen. Angeborene Contracturen der Finger und Klinodaktylien. *Arch. f. Orthop. u. Unfall.-Chir.*, xxvi. 126-137, figs. 7.
ZARFL, M. 1921. Über die morphologische Bedeutung der blauen Geburtsflecke (Mongolenflecke). *Zeits. f. Kinderheilk.*, xxxi. 80-97.
ZARFL, M. 1926. Neue Beiträge zum Studium der blauen Geburtsflecke (Mongolenflecke). *Zeits. f. Kinderheilk.*, xli. 356-369, figs. 3.
ZAVADOVSKY, M. M. 1926. Crosses between yak and zebu (Russian). *Trudi Labor. Exper. Biol. Zoopark. Moscow*, i.

LIST OF GENERAL WORKS BEARING ON HEREDITY IN MAN

BABCOCK, E. B., and CLAUSEN, R. E. 1918. Genetics in relation to agriculture. London and New York : Hill Publishing Co.

BATESON, W. 1913. Mendel's Principles of Heredity. Cambridge Univ. Press.

BAUR, E., FISCHER, E., and LENZ, F. 1923. Menschliche Erblichkeitslehre und Rassenhygiene (Second Edition). Munich : Lehmann.

CARR-SAUNDERS, A. M. 1922. The population problem. Oxford Press.

CASTLE, W. E. 1916. Genetics and Eugenics. Harvard Univ. Press.

CREW, F. A. E. 1925. Animal genetics. Edin. : Oliver and Boyd.

CREW, F. A. E. 1927. Organic Inheritance in Man. Edinburgh : Oliver and Boyd.

DAHLBERG, G. 1926. Twin births and twins from a hereditary point of view. Stockholm : Bokförlags-A.-B. Tidens Tryckeri.

DAVENPORT, C. B. 1911. *Heredity in relation to eugenics. London* : Williams and Norgate.

ELLIS, HAVELOCK. 1927. A study of British genius (Second Edition). London : Constable.

GALTON, F. 1869. Hereditary genius (Second Edition, reprint, 1914). London : Macmillan.

GALTON, F. 1883. Inquiries into human faculty and its development. London : Macmillan.

GALTON, F. 1889. Natural inheritance. London : Macmillan.

GATES, R. RUGGLES. 1915. The mutation factor in evolution. London : Macmillan.

GATES, R. RUGGLES. 1923. Heredity and Eugenics. London : Constable.

GODDARD, H. H. 1914. Feeblemindedness, its causes and consequences. New York, Macmillan.

GUYER, M. F. 1916. Being well-born. Indianapolis : Bobbs-Merrill Co.

HOLMES, S. J. 1923. Studies in evolution and eugenics. New York : Harcourt Brace and Co.

HOLMES, S. J. 1924. A bibliography of eugenics. *Univ. Calif. Publ. in Zool.*, vol. xxv.

MORGAN, T. H. 1926. The theory of the gene. New Haven : Yale Univ. Press.

NEWMAN, H. H., and others. 1925. Evolution, genetics, and eugenics. Univ. Chicago Press.

PEARL, R. 1925. Studies in human biology. Baltimore : Williams and Wilkins.

PEARSON, KARL, and collaborators. Treasury of human inheritance. Cambridge Univ. Press.

PLATE, L. 1913. Vererbungslehre, mit besonderer Berücksichtigung des Menschen, für Studierende, Ärzte und Züchter. Leipzig : W. Engelmann.

POPENOE, PAUL, and JOHNSON, R. H. 1920. Applied eugenics. New York : Macmillan.
PUNNETT, R. C. 1919. Mendelism (Fifth Edition). London : Macmillan.
SIEMENS, H. W. 1924. Die Zwillingspathologie. Ihre Bedeutung, ihre Methodik, ihre bisherigen Ergebnisse. Berlin : J. Springer.
SIEMENS, H. W. 1923. Einführung in die allgemeine und spezielle Vererbungspathologie des Menschen (Second Edition). Berlin : J. Springer.
WILSON, E. B. 1925. The cell in development and heredity (Third Edition). New York : Macmillan.

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